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Cervical Cancer Profile in dr. Cipto Mangunkusumo Hospital Year 2013

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Abstract

Background: Cervical cancer ranks in the second place based on the malignancy among female sex in Indonesia with a prevalence of 14.4% and a mortality rate of 10.3%. Hospital-Based Cancer Registry (HBCR) is a system of cancer registration in a hospital that can provide information about the general information of cancer patients, treatment, and outcome of treatment. This study was conducted to obtain the profile of cervical cancer in dr. Cipto Mangunkusumo general hospital (RSCM) in 2013 based on data from HBCR RSCM. **Methods:** The study was conducted by extracting the epidemiological data and cervical tumor data from HBCR RSCM in 2013 which was then analyzed descriptively. **Results:** The result showed that cervical cancer ranks at the second place from all the malignancy at RSCM (12%, n= 678), with domicile mostly come from outside Jakarta (52.8%, n = 358). The average age of cervical cancer was 49.48 years, the most common occurs in the age range 45-49 years. In terms of histopathology, squamous cell carcinoma is the most prevalent type of histopathology (74.2%, n = 447). The surgery is a type of action that done for early-stage cervical cancer (83,3%, n = 25), whereas the action of radiation is mostly done in locally advanced cervical cancer (79,9%, n = 273). **Conclusion:** Nevertheless, cervical cancer has a significant health burden in Dr. Cipto Mangunkusumo general hospital which is needed further management.

Keywords: cervical cancer; hospital-based cancer registry

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INTRODUCTION

Based on Indonesia Health Profile 2013, the prevalence rate of cancer in Indonesia was 1.4% with the highest in Yogyakarta (4.1%), Central Java (2.1%), Bali (2%) and Jakarta (1.9%).¹ According to WHO data in 2012, cervical cancer was the third most frequent cancer in women (9%) then followed by corpus uteri cancer and ovarian cancer in the fourth (7.1%) and sixth positions (3.4%). In Indonesia, cervical (14.4%), ovarian (6.1%) and uterine cancer (6%) were the second, third and fourth most frequent cancer in women. The mortality rate of cervical, ovarium and uterine cancer is 10.3%, 7.7%, and 2.1%. Estimated 500.000 cervical cancer patients all over the world and 233.000 patients died

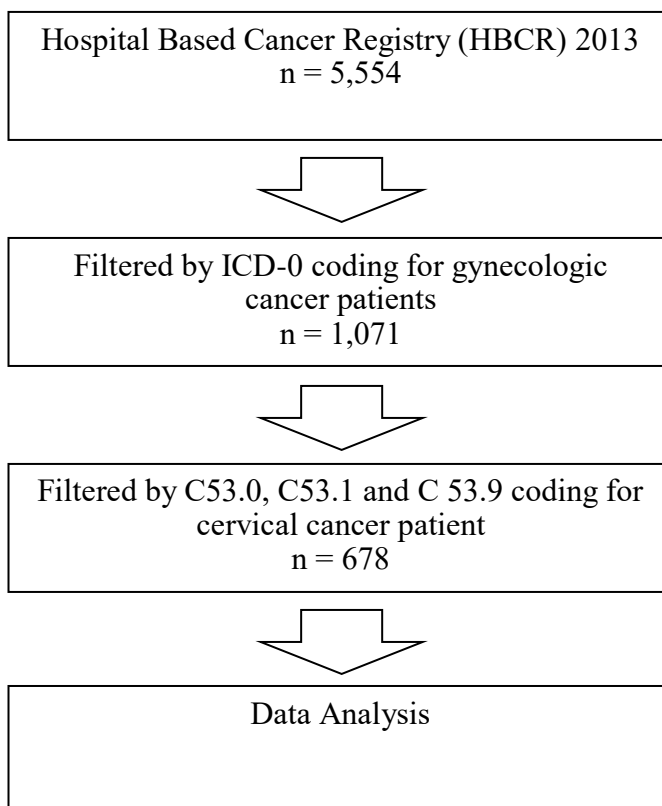
each year. In Indonesia, the incidence rate of cervical cancer is 13%. Approximately 90% of cervical cancer cases were related to Human Papilloma Virus (HPV) through sexual contact, HPV 16 and 18 which are commonly founded, while HPV 31,33,35,39,45,51,52,56 and 58 are less frequently found.^{3,4} Based on The Indonesian National Health Insurance System data during period January until June 2014, reported that cancer treatment took second place with 88,106 cases and 124,7 billion rupiahs, while for inpatient patients took fifth place with 56,033 cases and 313,1 billion rupiahs. The treatment of cervical cancer is based on FIGO staging. For stage 1A1, surgery may be performed as a

definitive treatment, stage 1A2 to IIA can be treated with surgery or radiation therapy, the study shows no difference result between them. For stage IIB to IVA, radiation therapy with concurrent chemotherapy is recommended. Brachytherapy with External Beam Radiation Therapy may also recommended for recurrent cases. Concurrent chemotherapy with External Beam Radiation Therapy enhance local control, reduce the risk of distant metastatic and improve Disease-Free Survival (DFS) and Overall Survival.⁴ For cervical cancer patient stage 1A2, 1B2 and IIA, radical hysterectomy followed by adjuvant pelvic radiation with or without concurrent chemotherapy, showed improvement of 4-year overall survival rate 71% for radiation only and 81% for chemoradiation.⁶

While for cervical cancer patient stage IIB to IVA, radiation with concurrent chemotherapy has been shown improve Progression-Free Survival and Overall Survival.⁷ National Guideline of Medical Services for Cervical Cancer is a guideline that was made based on data and consensus of expert contributors for the current management of cervical cancer. It can be specifically used as a guide in cervical cancer patients without other diseases or complications to improve the patient results of therapy.⁸ Hospital-Based Cancer Registry (HBCR) is a cancer registration system conducted in hospitals. HBCR provides information about cancer patients, treatment and results. In general, the aim of HBCR is to assess a nursery of cancer patients, clinical studies to evaluate therapeutic responses, pattern of metastatic spread and facilities planning. Specifically, HBCR contributes to the active follow-up of cancer patients, survival rate related anatomical location, clinical-stage, illustrates trend proportion in early and advanced stages when patients are diagnosed and help to assess the quality of hospital services and cancer services surrounding hospitals. HBCR is obtained from the registration process (abstraction and verification) with a standardized system.⁹ Based on the data above, epidemiological information related cervical cancer is needed as a reference in the cervical cancer service system in RSUPN Dr. Cipto Mangunkusumo, especially to determine the priority services and find out the success rate of the implemented program. In addition, authors also want to know the relation between the performed treatments compared to National Guideline of Medical Services for Cervical Cancer. Therefore authors intend to conduct a study of Cervical Cancer Profile in RSUPN Dr. Cipto Mangunkusumo Based On HBCR.

METHODS

A retrospective study was conducted by recruiting all cancer patient that registered at Hospital Based Cancer Registry (HBCR) in 2013 (n=5,554) then filtered by ICD-0 coding (n=1,071), C53.0, C53.1 and C53.9 coding for cervical cancer patient (n=678). The data was then analyzed descriptively.



RESULTS

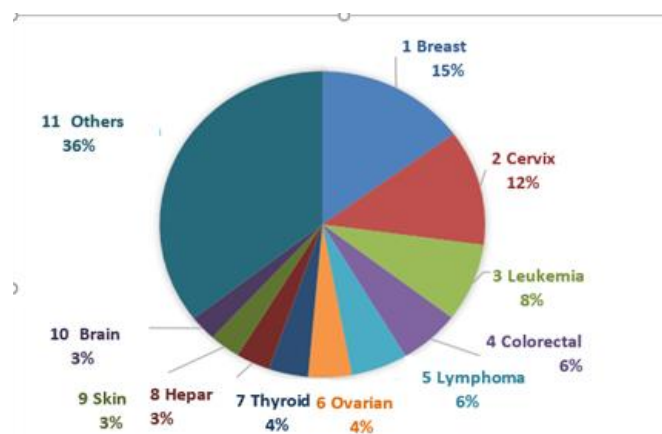


Figure 4.1. The Distribution of 10 Most Common Cancer Cases in RSUPN dr. Cipto Mangunkusumo (n=5,554)

According to HBCR RSCM 2013, the third most frequent cancer in RSCM during 2013 was breast cancer (15%, n=830), cervical cancer (12%, n=678) and leukemia (8%, n=459). The fifth and sixth places are colorectal cancer and lymphoma.

Cervical cancer (63.4%, n=678) was the most frequent cancer among gynecologic cancers (19%, n=1,071), followed by ovarian cancer (23.3%, n=239) and uterine cancer (10.2%, n=109), while vaginal cancer (1.3%, n=14) and vulvar cancer (1.2%, n=13) took the fourth and fifth position.

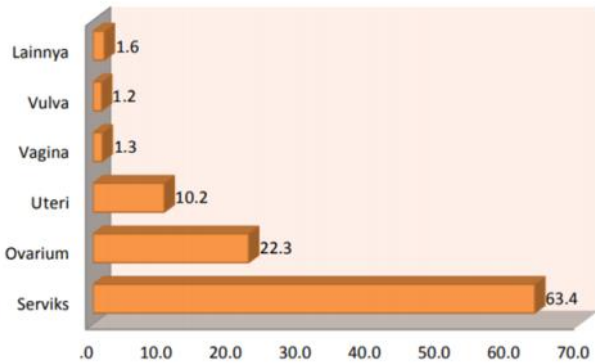


Figure 4.2. The Distribution of Gynecologic Cancers in RSUPN Dr. Cipto Mangunkusumo during 2013

Figure 4.3 showed most of the cervical cancer patients in RSUPN Dr. Cipto Mangunkusumo come from outside Jakarta (52.8%, n=358), while 47.2% (n=320) from Jakarta. Figure 4.4 showed 30.8% (n=209) from outside Jakarta is dominated by the patients from Bogor Depok, Tangerang, and Bekasi (Bodetabek), while 11.9% (n=81) from outside Java Island.

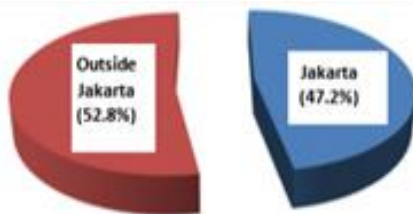


Figure 4.3. The Domicile Distribution of Cervical Cancer Patients in RSUPN Dr. Cipto Mangunkusumo

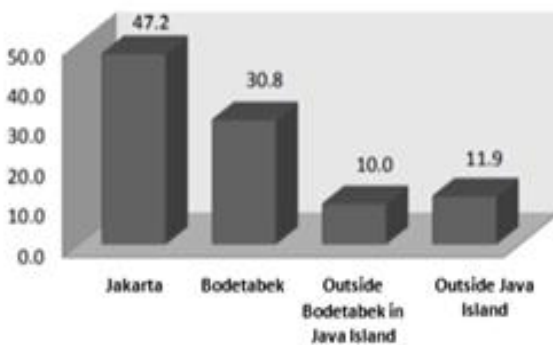


Figure 4.4. The Domicile Distribution of Cervical Cancer Patients from Outside Jakarta in RSUPN Dr. Cipto Mangunkusumo

Figure 4.5 showed the age distribution of cervical cancer patients in RSUPN Dr. Cipto Mangunkusumo. It occurs commonly in the age range 45-49 years (20.4%,

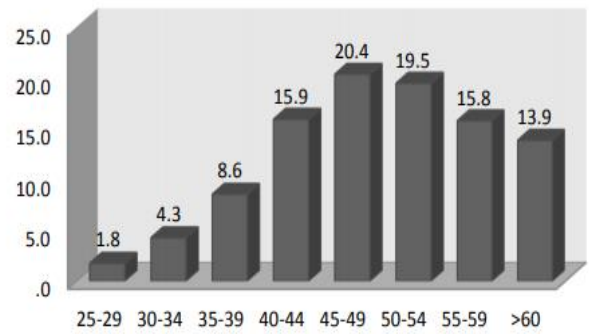


Figure 4.5. The Age Distribution of Cervical Cancer Patients in RSUPN Dr. Cipto Mangunkusumo

Malayan was the most frequent races in cervical cancer patients (39.8%, n=270), while 1.9% (n=12) was non-Malayan. Others (58.3%) were unknown.

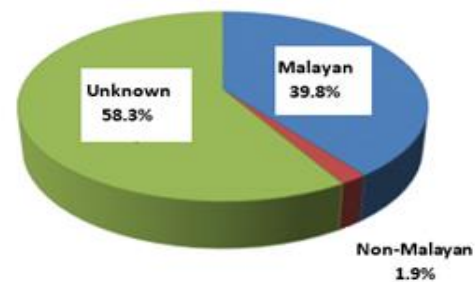


Figure 4.6. The Racial Distribution of Cervical Cancer Patients in RSUPN Dr. Cipto Mangunkusumo

Figure 4.7 showed 85.2% (n=255) was housewife, followed by officer (8.4%, n=25). Others were unknown.

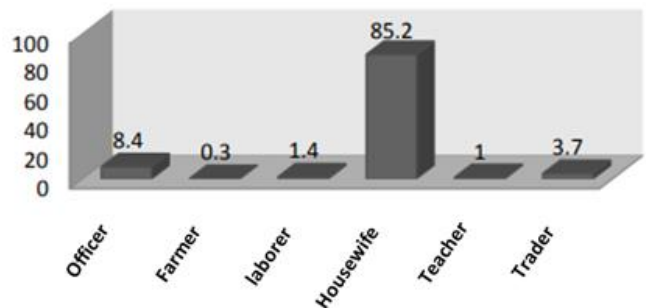


Figure 4.7. The Occupational Distribution of Cervical Cancer Patients in RSUPN Dr. Cipto Mangunkusumo

Histopathology was commonly used to diagnose cervical cancer (93.7%, n=635), followed by clinical diagnosis (3.1%, n=21) and Laboratory or radiology diagnosis (2.5%, n=17)

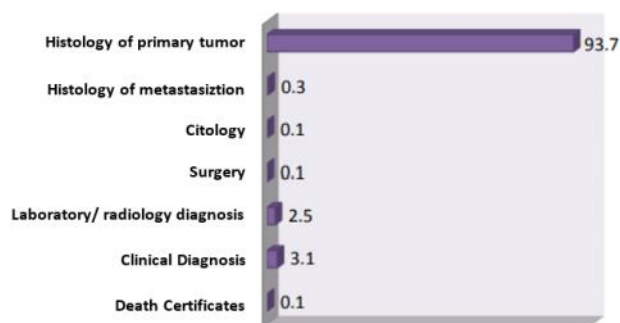


Figure 4.8. The Distribution of Cervical Cancer Diagnosis in RSUPN Dr. Cipto Mangunkusumo

Based on histopathology test results, squamous cell carcinoma was the most frequent (74.2%, n=447), especially non-keratinizing type squamous cell carcinoma (50.5%, n=304), then followed by adenocarcinoma (14%, n=84), adenosquamous carcinoma (6.8%, n=41), villous adenocarcinoma (0.2%, n=1) and sarcoma (0.2%, n=1).

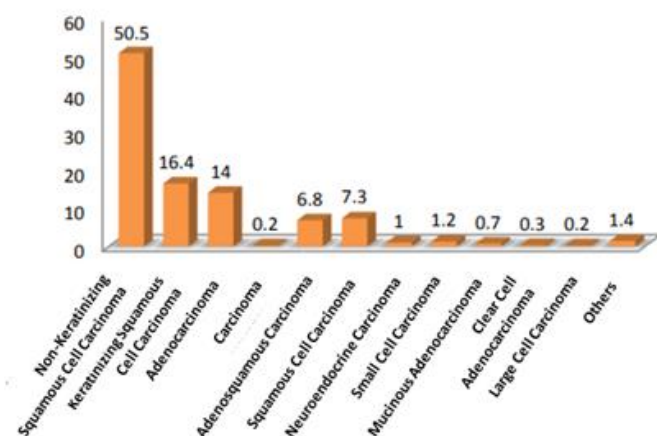


Figure 4.9. Morphology Distribution of Cervical Cancer Based on Histopathology Test in RSUPN Dr. Cipto Mangunkusumo

Moderately-differentiated was the most recently founded from the histopathology test (61%, N=244).

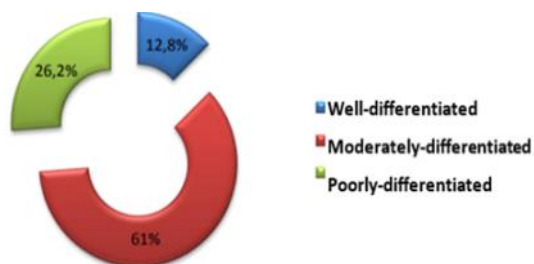


Figure 4.10. Morphology Grading Distribution of Cervical Cancer Based on Histopathology Test in RSUPN Dr. Cipto Mangunkusumo

Most cervical cancer patients in RSUPN Dr. Cipto Mangunkusumo are on stage IIIB (45%, n=260), followed by stage IIB (23.1%, n=133) and stage IB (10%, n=58).

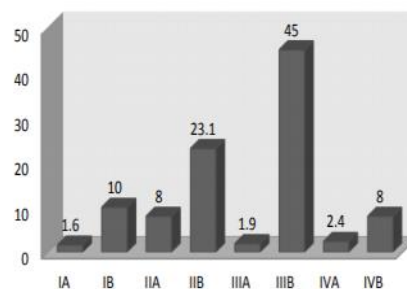


Figure 4.11. Cervical Cancer Stage Distribution Frequency in RSUPN Dr. Cipto Mangunkusumo

Table 4.1 showed most cervical cancer patients were treated with radiation (83.2%, n=397), while surgery (8.8%, n=42).

Table 4.1 Treatment Distribution of Cervical Cancer Patients in RSUPN Dr. Cipto Mangunkusumo 2013

Treatment	Number of Patients	Percentage
Surgery	42	8.8
Radiation	397	83.2
Chemotherapy	38	8

Table 4.2 showed 442 of 678 cervical cancer patients were treated with operation/ radiation/ chemoradiation/ chemotherapy, while 236 patients were treated with other treatments, referred to other hospitals and loss to follow up.

Table 4.2 Treatment by Stage of Cervical Cancer Patients in RSUPN Dr. Cipto Mangunkusumo 2013

Stage	Radiotherapy /Surgery/ Chemotherapy	Others	Frequency
IA	4	5	9
IB	40	18	58
IIA	26	20	46
IIB	91	42	133
IIIA	6	5	11
IIIB	185	75	260
IVA	6	8	14
IVB	31	15	46
Non-identified Frequency	53	48	101
	442	236	6

Table 4.3 showed surgery was the most frequent treatment to the early-stage cervical cancer patients (83.3%, n=25) with most of them on stage IB (56.7%, n=17) and stage IA (13.3%, n=4) from 39 patients who were treated with surgery. There was no patient with stage IIIA, IIIB, IVA, and IVB treated with surgery. Radiation may be performed for the cervical cancer patient local late stage (79.9%, n=273) with most of them on stage IIIB (52.3%, n=179) and stage IIB (24.3%, n=83).

Table 4.3 Treatment By Stage Distribution of Cervical Cancer Patients in RSUPN Dr. Cipto Mangunkusumo 2013

Treatment	Staging							
	IA	IB	IIA	IIB	IIIA	IIIB	IVA	IVB
Surgery	13.3/ 4	56.7/ 17	13.3/ 4	16.7/ 5	0	0	0	0
Radio therapy	0	6.7/2 3	5.8/2 0	24.3/ 83	1.5/ 5	52.3 /179	1.8/6	7.6/ 26
Chemo therapy	0	0	11.7/ 2	17.6/ 3	5.9/ 1	35.3 /6	0	29.5 /5

DISCUSSION

Table 4.1 shows- cervical cancer (12%, n=678) was the second most frequent cancer among all cancers in RSCM in 2013, while it was the most frequent cancer (63,4%) among gynecologic malignancies. Cervical cancer still a significant health burden in RSUPN Dr. Cipto Mangunkusumo which is needed a further plan of action. According to WHO data 2012, in Southeast Asia, cervical cancer is the second most frequent cancer with the prevalence rate 14.2% and incidence rate 10.2%, while the most common cancer among gynecologic malignancies with prevalence rate 22.8% and incidence rate 19.3% followed by ovarian and endometrial cancer. In Malaysia, it took first position with prevalence rate 12.7%. INASGO stated that cervical cancer is the most frequent cancer among all gynecologic malignancies in Indonesia then followed with ovarian and endometrial cancer.¹⁴ In our study, 52.8% patients are from Jakarta, 30.8% of them from Bogor, Depok, Tangerang, and Bekasi (Bodetabek), it is caused by easy healthcare access. Hospital facilities affect cancer services such as surgery, chemotherapy, and radiation. RSUPN Dr. Cipto Mangunkusumo is a national referral center that performs cancer services from diagnosis to management. There are 30.8% (n=209) patients are from outside Bodetabek, 11.9% (n=81) are from outside of Java Island. Cancer Registry Report from Goiania, Brazil from 1998 to 2004 showed

the average age of cervical cancer patients is 45-50 years. In India, the peak of incidence is in 55-59 Years. HPV infections are widely spread all around the world with the peak incidence in the age of 25-35 years, the age of highly sexual activities.^{3,16} In 10 to 20 years, cervical cancer may be developed after the first exposure. In Ulaanbaatar, Mongolia, 35% of cervical cancer patients are the age 15-59 years, which 48.4% of them are less than 25 years. HPV infection decreased by increasing age.¹⁷ In our study, frequency distribution same with the literature with the peak of incidence 45-49 years. Christopher explained that incidence and cervical cancer survival are not related with races such as African, Caucasoid, Hispanic and Asian.¹⁸ Mund et al stated that African cervical cancer patients stage IB to IIIB who treated with radiation have a less survival rate than Caucasoid (60% vs 47.9%), but this study is not statistically significant. It is still needed further studies about relation between cervical cancer incidence, comorbidity, socioeconomic status, and treatment. Monk et al stated that there is a relation between race, pathological factors, and survival rate. Age, staging and tumor grading are the predictors of disease-free survival and overall survival in multivariate analysis but not affected by races.^{19,20,21} In Indonesia, Malayan is the most dominant race. In our study, Malayan are the most common races (39.8%) and other races such as Tionghoa, Caucasoid, Hispanic, and African are in a small frequency. According to Statistic Center results in 2013, there are 36.036.779 housewives and 45.827.785 officers. In our study, 255 cervical cancer patients are housewives and 25 patients are officers. Finnish reported that risk of cervical cancer patients increases 20-40% in patients who contacted aliphatic, alicyclic, aromatic, chlorinated hydrocarbons compounds, silica and sawdust. Weiderpass reported that cervical cancer related to aliphatic and acyclic compounds (RR=1.3, n=91), aromatic (RR=1.2, n=318), chlorinated hydrocarbons solvents (RR=1.3, n=50), silica (RR=1.2, n=251) and sawdust (RR= 1.21, n=249).^{22,23} According to literature above, housewives and officers are the risk factor of cervical cancer. 299 of 678 patients' occupational status in our study are not known. We can not conclude because of the limit of data.

There is seven histopathology type of cervical cancer, squamous cell carcinoma (keratinized and non-keratinized), endometrioid adenocarcinoma, clear cell carcinoma, adenosquamous carcinoma, adenoid cystic carcinoma, small cell carcinoma, and undifferentiated carcinoma.²⁴ Squamous cell carcinoma is the most frequent cancer (80%). 10-20% cervical cancer patients

are adenocarcinoma from endocervix gland, which has high recurrence rate and low survival rate.²⁵ Clear cell carcinoma is adenicarcinoma variant that related to diethylstilbestrol (DES). Other histology like neuroendocrine carcinoma, mixed mesodermal tumors and lymphoma are less founded.^{4,10} In our study, 74.2% (n=447) are the most frequent cancer then followed by adenocarcinoma (14%, n=84) and adenosquamous carcinoma (6.8%, n=41), these results are same with other literature. Based on differentiation stage, moderately differentiated cancers are the most frequent (61%, n=244). Most literature stated there is no correlation between the progress of tumor and differentiation stage in squamous cell carcinoma and adenocarcinoma. Reagan and Fu reported prognostic value of histology differentiation in patients who are treated with radiation. In chemoradiation era, Monk et al reported that patients who are treated with surgery are not related to the stage of cancer. Cervical cancer patients who come to RSCM 2013 are commonly on stage IIIB (45%, n=260) and stage IIB (23.1%, n=133). In India, 50% of cervical cancer patients who come to hospital are on stage III.²⁷

The choice of treatment for cervical cancer patients depends on FIGO staging. For stage IA1, surgery may be performed as a definitive treatment, stage IA2 to IIA can be treated with surgery or radiation therapy, the study shows no difference result between them. For stage IIB to IVA, radiation therapy with concurrent chemotherapy is recommended. Brachytherapy with External Beam Radiation Therapy may also recommended for recurrent cases. Concurrent chemotherapy with External Beam Radiation Therapy enhance local control, reduce the risk of distant metastatic and improve Disease-Free Survival (DFS) and Overall Survival.^{4,10} According to National Guidelines of Medical Services for Cervical Cancer 2016, the choice of treatment of patients stage IA2, IB1 and IIA1 are radical hysterectomy with pelvic lymphadenectomy followed with adjuvant radiation or chemoradiation (patient with risk factors or surgery cannot be performed). Neoadjuvant chemotherapy (three serial) followed with radical hysterectomy and pelvic lymphadenectomy or ultraradical hysterectomy may be performed. Chemoradiation and radiation are recommended for patient stage IIIA and IIIB.⁸ Murat stated that early micro-invasive cancer (stage IA1) is treated with conservative surgery, while early invasive cancer (stage IA2, IB1 and some IIA1 with small size tumor) there are no different result between radical operation and radiation. For the locally advanced cancer (IB2, IIB, IIIA, IIIB, and IVA) are treated with

chemoradiation, while systemic therapy is the choice of treatment in advanced cancer (stage IVB).²⁸ In our study, radiation is the most common treatment (83.2% , n= 397), while 8.8% (n=42) are treated with surgery. Most of patients came to RSUPN Dr. Cipto Mangunkusumo are on locally advanced stage (72.4%) and early-stage (19.6%). Surgeries are dominantly done in early-stage patients (83.3%, n= 25), while radiations are the choice of treatment in locally advanced cancer. These results show no different from other literature and National Guideline of Medical Services for Cervical Cancer.

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