



# Radioterapi & Onkologi Indonesia

Journal of Indonesian Radiation Oncology Society



## Profile of Cervical Cancer Management with Radiation and Chemoradiation Therapy at The Radiotherapy Installation of RSUP Dr. Mohammad Hoesin Palembang

Wahyudi Nurhidayat<sup>1</sup>, Dini Andriani<sup>1</sup>, Lucky Taufika Yuhedi<sup>1</sup>, Wahyu Diyana<sup>1</sup>

<sup>1</sup>Radiation Oncologist, Department of Radiotherapy, Mohammad Hoesin Central General Hospital, Palembang, Indonesia

Article information:

Received: December 2023

Accepted: January 2024

Correspondence:

Wahyudi Nurhidayat

Mohammad Hoesin Central  
General Hospital, Palembang,  
Indonesia

Email:

vanderwates@gmail.com

### Abstract

Cervical cancer is a gynecologic malignancy that ranks as the second most common cancer affecting women, following breast cancer. Recommended therapy for locally advanced cervical cancer, according to PNP (National Guidelines for Cancer Services) is chemoradiation or radiotherapy. The aim of this study is to present a comprehensive analysis of the management cervical cancer with chemoradiation and radiation therapy, which will allow for a comparison of outcomes, specifically the clinical tumor response and radiation-related side effects, in patients with locally advanced cervical cancer who received either radiation therapy alone or a combination of chemoradiation. This research is a retrospective observational study using our hospital database in 2022. SPSS was used for the data analysis. The study findings indicated a notable disparity between chemoradiation therapy and radiation alone in terms of treatment outcomes for patients with stage III cervical cancer, with a p-value of 0.011. The findings of this study indicate that the projected number of new cervical cancer cases at the RSMH Palembang Radiotherapy Installation in 2022 was 194 patients. The age ranged from 27 to 75 years, with an average age of  $49.59 \pm 9.29$  years. A significant proportion, specifically 42%, of the domicile addresses of most patients originate from Palembang City and its surrounding areas. Stage III was the most advanced stage of patients, with a prevalence of 76%. The distribution of cervical cancer cell types was predominantly squamous cell carcinoma, accounting for approximately 80%, with adenocarcinoma comprising the remaining 20%. The overall efficacy of therapy for cervical cancer, regardless of the stage, was 63.5%.

**Keywords:** Profile Cervical cancer, Chemoradiation, Radiation

Copyright ©2024 Indonesian Radiation Oncology Society

### Introduction

The prevalence of cancer is steadily rising. According to data from GLOBOCAN, the International Agency for Research on Cancer (IARC), there were 21 million new instances and 10.5 million mortalities attributed to cancer in 2018.<sup>1</sup> According to the 2013 Riskesdas data, the cancer incidence rate in Indonesia is 1.4 per 1000 population, with an estimated total of 347,792 cases.<sup>2</sup> WHO data for 2020 shows that the death rate caused by cancer in Indonesia reached 52.79% for men and 47.20% for women.<sup>3</sup> In Indonesia, according to WHO data, cervical cancer ranks second in cancer cases in women after breast cancer. The number of new cases of cervical cancer is around 20,928, and deaths due to cervical cancer are 10.3%.<sup>4</sup> Based on data from the Indonesian Ministry of Health in 2010, the incidence of cervical cancer was 100 per 100,000 population per year.<sup>5,6</sup>

Cervical cancer is the most common malignancy in the female reproductive organs, of which

more than 90% is caused by infection with the Human Papilloma Virus (HPV). The HPV infection process takes quite a long time to become cervical cancer, namely 10–20 years. Cervical cancer treatment options include a combination of surgery, chemotherapy, and radiation.<sup>5–7</sup> Based on the NCCN, the choice of therapeutic modality for cervical cancer is based on its stage. In locally advanced stages, the main treatment is a combination of chemotherapy and radiation, often called chemoradiation.<sup>8</sup>

Standard chemotherapy is carried out every week with a cisplatin drug regimen at a dose of 40 mg/m<sup>2</sup>. The standard radiation therapy for locally advanced cervical cancer is external radiation and brachytherapy. The recommended radiation dose for definitive curative therapy is 80–85 Gy, of which 45–50 Gy with external radiation and 30–40 Gy with brachytherapy. The latest radiation equipment, namely the "linear accelerator" or Linac and tomotherapy with advanced radiation techniques such as IMRT, VMAT,

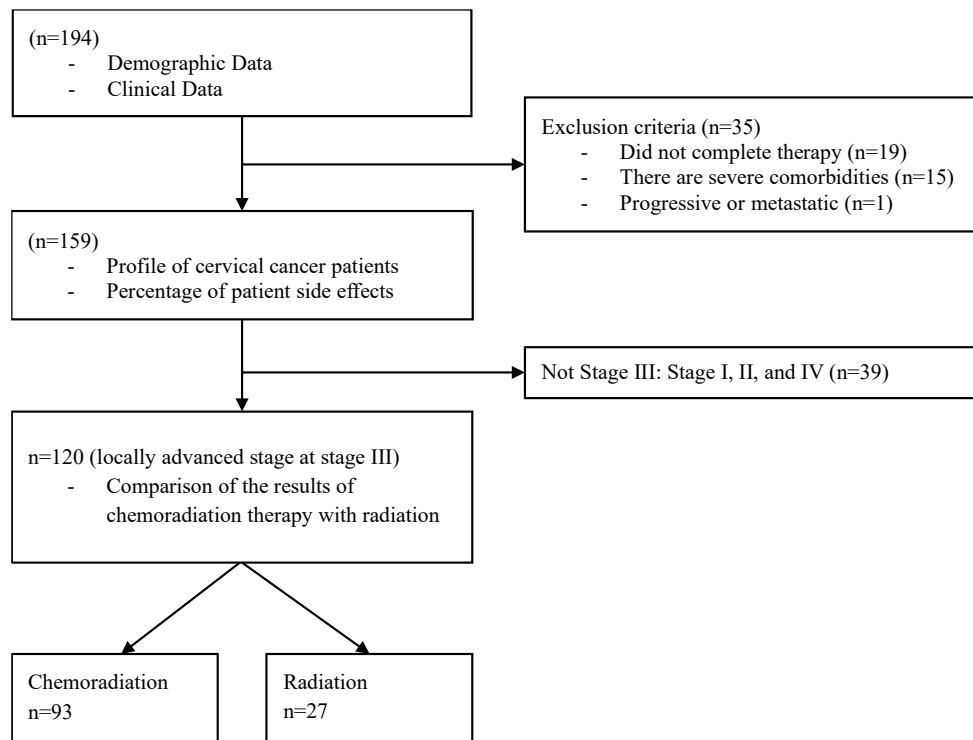


Figure 1. Cervical cancer study flowchart.

and IGRT, can provide radiation with a higher level of accuracy, so that the radiation dose given to the patient can be greater, but the dose at surrounding organs will be much lower.<sup>9-12</sup>

Based on the National Guidelines for Medical Services (PNPK) for Cervical Cancer, the recommendation for locally advanced stages (stage IIB - IIIB) is chemoradiation or radiotherapy only.<sup>5,6</sup> Klop et al. have reported that administering chemoradiation to patients with locally advanced cervical cancer can enhance both local cancer control and patient life expectancy.<sup>10</sup> This result in line with study by Datta et al, and Eifel et al.,<sup>11,12</sup> However, unfortunately these positive results were also accompanied by an increase in acute side effects in patients in the form of anemia and leukopenia.<sup>11,12</sup> Radiation therapy is sometimes administered to patients due to a variety of reasons, including declining kidney function, patient and family rejection of chemotherapy, and medication limitations. The treatment process for patients with cervical cancer, especially those in locally advanced stages, is also influenced by other factors, such as limited radiation equipment, long wait times for radiation services, and a lack of protocols for chemoradiation implementation in a center or hospital. These variables interact and affect the way patients respond to treatment, how well they do, and whether they develop side effects.

In this study, we compared the management profile of locally advanced cervical cancer therapy using radiation alone with chemoradiation at the RSUP dr. M. Hoesin Palembang in the 2022 period along with demographics, patient characteristics and side effects that occurred during cervical cancer therapy.

## Material and Methods

This was a retrospective cohort study using data collected from medical records between January and December 2022. Data on patient demographic, treatment side effects, and clinical response were taken and presented in this paper. Data was analyzed using the chi square test in the SPSS version 21 software.

The sample for this study was all patients with locally advanced cervical cancer who underwent treatment in the form of chemoradiation and radiation in 2022. In collecting and processing demographic data on cervical cancer patients, all patients were included for analysis.

To analyse the differences on treatment outcomes and side effects, only patients who met the criteria below were included. The inclusion criteria are:

1. Patients with stage III cervical cancer at the RSMH Palembang Radiotherapy Installation, namely stages IIIA, IIIB, IIIC
2. Have complete clinical data and therapy data in the medical record or EMR.
3. PA examination results: squamous cell carcinoma and adenocarcinoma

The exclusion criteria for this study are:

1. Have a history of previous cancer treatment, such as chemotherapy and/or radiation (residual or inadequate therapy)
2. There are serious comorbid diseases that worsen the results of cancer treatment ect: uncontrolled hypertension and or diabetes mellitus, chronic kidney disease, etc.
3. Not completing the research until the end of the evaluation

The SPSS version 21 was employed to conduct statistical analysis, which reported patient profile data in the following formats: age, address, tumor stage, and treatment group. Additionally, clinical responses to radiation treatment and the occurrence of side effects during therapy were compared between the radiation-only patient group and the chemoradiation patient group. Internal examination of cervical cancer patients at the time of their most recent brachytherapy to assess their clinical response.

The RTOG (Radiation Therapy Oncology Group) score was used to assess the severity of radiation side effects once every five fractions which assessed by a radiation oncologist.

## Result and Discussion

In year 2022, RSMH Palembang's Radiotherapy Department has treated 194 cervical cancer patients. This data was processed to present patient demographic information, including age and address. The data was filtered using exclusion criteria, which included patients who did not complete therapy, severe comorbid diseases, and progressive disease conditions. As a result, there were 159 patients, of which presented as patient profile data in the form of cancer stage, histology type, and adverse effects. Meanwhile, among of them, there were 120 diagnosed with stage III, consisting of 93 receiving chemoradiation therapy and 27 with radiation therapy alone (Picture 1).

According to the patient demographic data (table 1), the age range varied from 27 to 75 years, with an average age of  $49.59 \pm 9.29$  years. The highest percentage, 40.2%, was found in the age group corresponding to the fifth decade. According to previous studies conducted by Yuski Amin et al at from Soetomo Hospital Surabaya and Anggraeni et al at from Cipto Mangunkusumo Hospital, the average age of patients with cervical cancer was 51 years.<sup>13,14</sup> In a multicenter study conducted by Kato et al, which included multiple countries in East Asia and Southeast Asia, including Indonesia, it was found that the average age of cervical cancer patients with stage IIB-III B was 51 years, with an age range of 28 to 70 years.<sup>15</sup> There has been a decrease in the average age of patients, with a shift towards younger individuals. This can be attributed to various factors, such as shifts in behavior, particularly increased promiscuity among adolescents, expedited availability of healthcare services, and alterations in the dissemination of information through the internet. In addition, traditional factors continue to have an impact as a result of a decline in the body's immune system, more potent viral factors, and the high prevalence of sexually transmitted infections.<sup>16</sup>

The patient addresses were divided into three groups, with the majority of them in group one: Palembang City, Banyuasin Regency, Ogan Ilir Regency, and Prabumulih City. The distance from the

Table 1. Demographic data of cervical cancer patients.

Variable	n= 194	
Age group	Noun	%
20-29	2	1
30-39	23	11.9
40-49	78	40.2
50-59	59	30.4
60-69	28	14.4
70-79	4	2.1
Patient address group		
Palembang, Banyuasin, Prabumulih, Ogan Ilir	82	42.3
South Sumatra Province other than Group 1	78	40.2
Outside South Sumatra Province	34	17.5
<b>Stadiums</b>	n =194	
I A	1	0.5
I B	5	2.6
II A	6	3.1
II B	20	10.3
III A	16	8.2
III B	90	46.4
III C	42	21.6
IV A	9	4.6
IV B	5	2.6
<b>Types of Cancer Cells</b>	n =194	
Adenokarsinoma	39	20.1
Clear cell carcinoma	1	0.5
Squamous cell carcinoma	154	79.4
<b>Therapy Group</b>	n =159	
Chemoradiation	117	73.6
Radiation	42	26.4
<b>Therapy Results</b>	n =159	
Complete response	101	<b>63.5</b>
Partial response	58	36.5
<b>Skin side effects</b>	n =159	
grade 0	6	3.8
grade 1	115	72.3
grade 2	37	23.3
grade 3	1	0.6
<b>Gastrointestinal Side Effects</b>	n =159	
grade 0	57	35.8
grade 1	81	50.9
grade 2	18	11.3
grade 3	3	1.9
<b>Urinary Tract Side Effects</b>	n =159	
grade 0	144	90.6
grade 1	12	7.5
grade 2	2	1.3
grade 3	1	0.6

patient's home to RSMH is less than 3 hours, and the use of a toll road speeds up the journey. Patients in Group One do not need to look for a halfway house and can commute to RSMH every day. Their accommodation costs will be lower in the city, and they will have to stay in a halfway house until they finish treatment, as opposed to patients who come from outside the area. The distance between patients and RSMH remains the most significant barrier to treating diseases, including cancer, given that the distance between districts and provinces on Sumatra is quite long, taking approximately 7-8 hours by road. These findings are consistent with study conducted Srinath et al, which found that educational factors, family support, and distance or ease of access all influence treatment compliance and success in cancer patients.<sup>16</sup>

The most common cancer stage was IIIB, with 90 patients (46.4%), meanwhile the total stage III were 148 patients, or 76.2%. Cervical cancer in Stage III is considered locally advanced. This is consistent with previous research, including studies by Amin et al, Lasut et al, Legianawati et al, and Watulinggas et al, which found that the majority of cervical cancer cases were locally advanced, particularly stages II and III.<sup>13,17-19</sup> The main cause is that Indonesian people do not understand efforts to prevent and early detect cervical cancer. This is in accordance with the study by Kurniawati et al, that 62.5% of cervical cancer patients have never had a pap smear, as an early detection examination for cervical cancer, and have never been given the HPV vaccination to prevent the incidence of cervical cancer.<sup>20</sup>

The types of anatomical pathology of cervical cancer cells in this study were squamous cell carcinoma, 79.4%, adenocarcinoma 20.1%, and clear cell carcinoma and 0.5%. This result is almost the same as previous studies conducted by Anggraeni et al, and Dwipoyono et al, that the histology of cervical cancer with squamous cell carcinoma type was 77% and adenocarcinoma 15%.<sup>14,21</sup>

Perez and Brady's as well as in William Gynecology, also reported that the squamous cell carcinoma cell type in cervical cancer is around 85% and the adenocarcinoma type is around 10- 15%.<sup>14,21-23</sup>

Of the 159 cervical cancer patients undergoing treatment at RSMH Palembang in 2022, it was found at the end of treatment that 101 patients had achieved a complete response. Overall, the success rate of therapy for cervical cancer at all stages was 63.5%. There was a significant difference between chemoradiation therapy and radiation and treatment outcomes in stage III cervical cancer patients, with  $p = 0.011$ . There was no difference in histological type in response to therapy with  $p > 0.05$ . The most common acute side effects of radiation that occurred in patients were first-degree skin side effects at 72% and first-degree gastrointestinal side effects at 51%. This result is in line with many previous studies, such as studies by Rose et al, Moris et al, and Eifel et al, which stated that chemoradiation is superior

to radiation therapy alone.<sup>24-28</sup> However, this success rate is accompanied by an increase in the incidence of acute side effects, which appear to be temporary.<sup>24-28</sup> There were serious or third-degree side effects, but the percentage was low, about 1% or less. In general, side effects on the skin and gastrointestinal tract can be overcome by providing symptomatic therapy. Further research is needed to assess other more serious side effects.

## Conclusions

The number of new cervical cancer patients at the RSMH Palembang undergoing chemoradiation and radiation in 2022 was 194 patients. The youngest was 27 years old and the oldest was 75 years old, with an average age of  $49.59 \pm 9.29$  years. Most patients' domicile addresses come from Palembang City and its supporting areas, about 42%. The highest stage of patients was stage III, which reached 76%. The proportion of cervical cancer cell types was squamous cell carcinoma, almost 80%, while adenocarcinoma was 20%. Overall, the success rate of therapy for cervical cancer at all stages was 63.5%. There was a significant difference between chemoradiation therapy and radiation and treatment outcomes in stage III cervical cancer patients, with  $p = 0.011$ . The most common acute side effects of radiation that occurred in patients were first-degree skin side effects at 72% and first-degree gastrointestinal side effects at 51%.

## References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* [Internet]. 2021;71:209-49. Available from: <https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21660>
2. Badan Penelitian dan Pengembangan Kesehatan. Laporan Riset Kesehatan Dasar (RISKESDAS) tahun 2013 dalam bentuk angka [Internet]. Badan Penelitian dan Pengembangan Kesehatan, editor. Jakarta: Badan Penelitian dan Pengembangan Kesehatan; 2013. Available from: <https://repository.badankebijakan.kemkes.go.id/id/eprint/4428>
3. World Health Organization (WHO). Cancer [Internet]. 2022 [cited 2022 Apr 1]. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer>
4. Surveillance Epidemiology and End Results Program (SEER). Cancer Stat Facts: Cervical Cancer [Internet]. National Cancer Institute (NCI). 2020 [cited 2022 Apr 1]. Available from: <https://seer.cancer.gov/statfacts/html/cervix.html>
5. Kementerian Kesehatan Republik Indonesia. Pedoman Nasional Pelayanan Kedokteran (PNPK) Tata Laksana Kanker Serviks [Internet]. Komite Penanggulangan Kanker Nasional, editor. Komite Penanggulangan Kanker Nasional. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018. Available from:

- <https://kemkes.go.id/id/pnpk-2018---tata-laksana-kanker-serviks>
6. Kementerian Kesehatan Republik Indonesia. Pedoman Nasional Pelayanan Kedokteran (PNPK) Tata Laksana Kanker Serviks. Komite Penanggulangan Kanker Nasional, editor. Jakarta: Kementerian Kesehatan Republik Indonesia; 2016.
  7. Andrijono, Purwoto G, Sekarutami SM, Handjari DR, Primariadewi, Nuhonni SA, et al. Panduan Praktik Klinis Kanker Serviks. 1.0.2018. Gondhowiardjo SA, editor. Jakarta: RSCM; 2018.
  8. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) - Cervical Cancer Version 1.2022. 1.2022. National Comprehensive Cancer Network (NCCN), editor. NCCN.org; 2022.
  9. Beyzadeoglu M, Ozyigit G, Ebruli C. Basic Radiation Oncology [Internet]. Second Edition. Basic Radiation Oncology: Second Edition. Switzerland: Springer International Publishing; 2022. 1–522 p. Available from: <https://link.springer.com/book/10.1007/978-3-030-87308-0>
  10. Klopp AH, Eifel PJ. Chemoradiotherapy for cervical cancer in 2010. *Curr Oncol Rep* [Internet]. 2011;13:77–85. Available from: <https://pubmed.ncbi.nlm.nih.gov/21042887/>
  11. Datta NR, Stutz E, Liu M, Rogers S, Klingbiel D, Siebenhüner A, et al. Concurrent chemoradiotherapy vs. radiotherapy alone in locally advanced cervix cancer: A systematic review and meta-analysis. *Gynecol Oncol* [Internet]. 2017 [cited 2024 Jul 21];145:374–85. Available from: <https://pubmed.ncbi.nlm.nih.gov/28188016/>
  12. Eifel PJ. Chemoradiotherapy in the treatment of cervical cancer. *Semin Radiat Oncol* [Internet]. 2006 [cited 2024 Jul 21];16:177–85. Available from: <https://pubmed.ncbi.nlm.nih.gov/16814159/>
  13. Amin Y, Mulawardhana P, Erwati D. Demografi, Respon Terapi dan Survival rate Pasien Kanker Serviks Stadium III-IVA yang Mendapat Kemoterapi Dilanjutkan Radioterapi. *Majalah Obstetri & Ginekologi* [Internet]. 2015;23:97–105. Available from: <https://garuda.kemdikbud.go.id/documents/detail/467160>
  14. Anggraeni TD, Nuranna L, Sobur CS, Rahardja F, Hia CW, Utami TW, et al. Distribution of Age, Stage, and Histopathology of Cervical Cancer: A Retrospective Study on Patients at Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, 2006-2010. *Indonesian Journal of Obstetrics and Gynecology* [Internet]. 2011 [cited 2022 Feb 14]; Available from: <http://inajog.com/index.php/journal/article/view/218>
  15. Kato S, Ohno T, Thephamongkhol K, Chansilpa Y, Cao J, Xu X, et al. Long-term follow-up results of a multi-institutional phase 2 study of concurrent chemoradiation therapy for locally advanced cervical cancer in east and southeast Asia. *Int J Radiat Oncol Biol Phys* [Internet]. 2013;87:100–5. Available from: <https://pubmed.ncbi.nlm.nih.gov/23920390/>
  16. Srinath A, Van Merode F, Rao SV, Pavlova M. Barriers to cervical cancer and breast cancer screening uptake in low- and middle-income countries: a systematic review. *Health Policy Plan* [Internet]. 2023;38:509–27. Available from: <https://pubmed.ncbi.nlm.nih.gov/36525529/>
  17. Lasut E, Rarung M, Suparman E. Karakteristik Penderita Kanker Serviks di BLU RSUP Prof. Dr. R. D. Kandou. *e-CliniC* [Internet]. 2015;3:83–6. Available from: <https://ejournal.unsrat.ac.id/v2/index.php/eclinic/article/view/6519>
  18. Legianawati D, Puspitasari IM, Suwantika AA, Kusumadjadi A. Profil Penatalaksanaan Kanker Serviks Stadium IIB–IIIB dengan Terapi Radiasi dan Kemoradiasi di Rumah Sakit Umum Pusat Dr. Hasan Sadikin Bandung Periode Tahun 2015–2017. *Indonesian Journal of Clinical Pharmacy* [Internet]. 2019;8:205–16. Available from: <https://jurnal.unpad.ac.id/ijcp/article/view/21795>
  19. Watulingas AM, Loho M, Wagey F, Manado SR, Obstetri B, Fakultas G, et al. Karakteristik penderita kanker serviks di RSUP Prof. Dr. R. D. Kandou Manado periode 1 Januari 2013 - 31 Desember 2015. *e-CliniC* [Internet]. 2016;4. Available from: <https://ejournal.unsrat.ac.id/v3/index.php/eclinic/article/view/14477>
  20. Kurniawati L, Nurrochmah S, Katmawanti S. Hubungan Antara Tingkat Pendidikan, Status Pekerjaan dan Tingkat Pendapatan dengan Usia Perkawinan Pertama Wanita di Kelurahan Kotalama Kecamatan Kedungkandang Kota Malang. *Preventia: The Indonesian Journal of Public Health* [Internet]. 2016;1:210–9. Available from: <https://journal2.um.ac.id/index.php/preventia/article/view/2748>
  21. Dwipoyono B, Nasdaldy N, Soemanadi S, Sjamsuddin S, Adisasmita A. Jenis Histologik dan Umur pada Kanker Serviks Uteri di Rumah Sakit Kanker “Dharmas.” *Indonesian Journal of Cancer* [Internet]. 2007;1. Available from: <https://www.indonesianjournalofcancer.or.id/e-journal/index.php/ijoc/article/view/1/1>
  22. Williamson JF, Brenner DJ. Perez and Brady’s principles and practice of radiation oncology. Seventh edition. Halperin EC, Wazer DE, Perez CA, Brady LW, editors. Perez and Brady’s Principles and Practice of Radiation Oncology. Philadelphia; Baltimore; New York: Wolters Kluwer; 2018. 530–581 p.
  23. Schorge JO, Schaffer J, Halvorson L, Hoffman B, Bradshaw K, Cunningham F. *William Gynecology*. 1st ed. Calver LE, editor. New York: McGraw-Hill Professional; 2008.
  24. Morris M, Eifel PJ, Lu J, Grigsby PW, Levenback C, Stevens RE, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med* [Internet]. 1999;340:1137–43. Available from: <https://pubmed.ncbi.nlm.nih.gov/10202164/>
  25. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* [Internet]. 1999;340:1144–53. Available from: <https://pubmed.ncbi.nlm.nih.gov/10202165/>

26. Eifel PJ. Concurrent chemotherapy and radiation: a major advance for women with cervical cancer. *J Clin Oncol* [Internet]. 1999;17:1334–5. Available from: <https://pubmed.ncbi.nlm.nih.gov/10334515/>
27. Ryu HS. Concurrent chemoradiotherapy in cervical cancer (a new paradigm in cervical cancer treatment). *Yonsei Med J* [Internet]. 2002;43:749–53. Available from: <https://pubmed.ncbi.nlm.nih.gov/12497658/>
28. Wang N, Guan QL, Wang K, Zhou X, Gao C, Yang HT, et al. Radiochemotherapy versus radiotherapy in locally advanced cervical cancer: a meta-analysis. *Arch Gynecol Obstet* [Internet]. 2011;283:103–8. Available from: <https://pubmed.ncbi.nlm.nih.gov/20157716/>