

## Determinants of Survival of Cervical Cancer: A Hospital Based Study

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Received date: April 8, 2017; Accepted date: May 8, 2017; Published date: May 15, 2017

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### Abstract

Globally uterine cervix cancer is one of the leading causes of death in females due to cancer, especially in developing countries. The aim of the study was to analyse the survival as well as understanding various prognostic factors for survival in patients of carcinoma cervix presenting in our hospital. A total of 508 patients were evaluated in radiotherapy department of Mahavir Cancer Sansthan and Research centre Patna, Bihar who came for follow up between April 2015 to March 2016 after completion of radical radiotherapy. Out of 508 patients 3.54% (n 18), 71.65% (n 364), 22.83% (n 116) and 1.9% (n 10) patients presented in stage I, II, III and IV A respectively. 53.54% of patients belonged to age group of 35 to 50 years with Survival of  $937 \pm 53.49$  days. 46.46% of the patients were more than 50 years age and their survival was  $933.3 \pm 57.12$  days. The mean duration for overall survival for all cases evaluated was  $957.4 \pm 39.49$  days. The mean duration for survival of stages I, II, III and IVA was  $1186 \pm 281.8$  days,  $960 \pm 85.04$  days,  $945.1 \pm 45.66$  days and  $765 \pm 181.5$  days respectively. Survival of patients having squamous cell carcinoma was  $970 \pm 42.89$  days and that of adenocarcinoma was  $669.5 \pm 120$  days and that of premenopausal and postmenopausal lady was  $997.5 \pm 79.28$  and  $940.1 \pm 45.39$  days respectively. It was evident from study that patients who presented in early stage had a better survival. There was no significant difference in survival of cervix cancer patients in different age groups while survival was greater in premenopausal cervical cancer patients.

**Keywords:** Cervical cancer; Survival; Histopathology; Radiotherapy

### Introduction

Globally uterine cervix cancer is one of the leading causes of death in females due to cancer, especially in developing countries where the mortality is 86% [1]. This high mortality is alarming and one needs to understand cervical cancer and its implications. India has the largest burden of cervical cancer patients as one in every 5th woman in the world suffering from cervical cancer belongs to India [2].

The main factor for prognosis and survival for cervical cancer is its staging at presentation [3,4]. Other factors responsible for survival are age at diagnosis, histological tumour type [5]. Persistent human papilloma virus (HPV) infection is the major cause for onset and development of cervical cancer [6]. Women with early sexual activity having early first pregnancy are at higher risk for developing cervical cancer. Apart from this low educational status, high parity and smoking are known risk factors for cervical cancer [7]. According to Mileschkin smokers have a greater risk for developing corpus invasive cervix cancer [8].

Radiotherapy is the mainstay of treatment as most of the patients present in advanced stages. Five year survival rates reported is 79%, 61%, 31% and 17% for stage I, II, III and IV respectively after taking into consideration of age, tumor bulk, anemia and renal failure [9]. The study of survival of cervical cancer patients is low in this part of the world. Thus present work is designed to study the factors associated with survival of cervical cancer patients treated in Bihar.

### Methods and Materials

A total of 508 patients were evaluated in radiotherapy outpatient department. Patients were of cervical cancer ranging from stage I to stage IV A as per FIGO classification. They had completed radiotherapy treatment by External Beam Radiotherapy (EBRT) as well as Intracavitary Radiotherapy (ICRT). Suitable patients also received concurrent chemotherapy. All those patients who came for follow up between April 2015 to March 2016 were evaluated. The study was approved by the ethics committee of Mahavir Cancer Institute and Research Centre, Patna, Bihar, India.

All patients underwent External beam Radiotherapy to pelvis at a doses of 50Gy for 25 fractions over a period of 5 to 6 weeks. All of them received intra cavitory radiotherapy in the doses of 7Gy for three fractions as per our institutional protocol. Chemotherapy consisted of weekly cisplatin  $40 \text{ mg/m}^2$  with premedication and adequate hydration. Patients who had completed their treatment and were on follow up were included. Every detail of them was taken from them as well as from their medical records right from the date of registration till their last follow up. Data was collected and statistical analysis was done with ANOVA test.

### Results

Out of 508 patients 3.54% (n 18), 71.65% (n 364), 22.83% (n 116) and 1.9% (n 10) patients presented in stage I, II, III and stage IV A respectively (Figure 1).

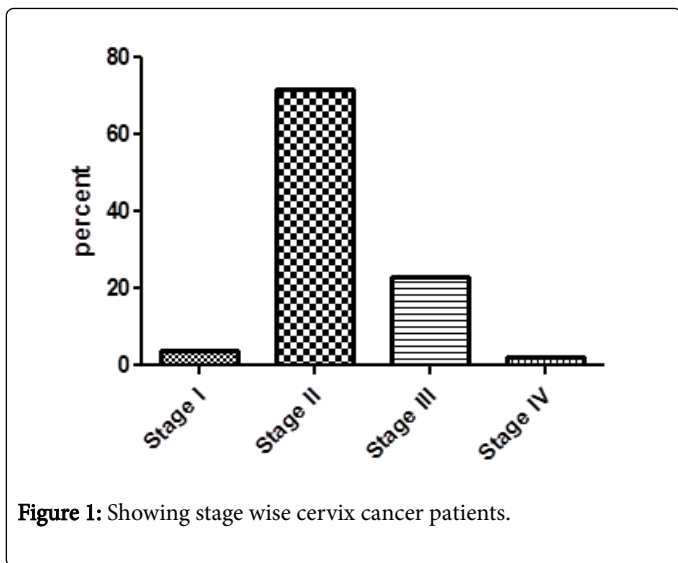


Figure 1: Showing stage wise cervix cancer patients.

The mean age for all the patients evaluated was 50.38 years with a median age of 50 years. 53.54% of patients belonged to age group of 35 to 50 years. Survival for this age group of patients was  $937 \pm 53.49$  days. 46.46% of the patients were of age more than 50 years and its survival was  $933.3 \pm 57.12$  days (Figure 2). The survival was slightly better in the younger age group. The mean age for premenopausal women was  $41.58 \pm 0.43$  years and for postmenopausal women was  $54.10 \pm 0.37$  years. The survival was  $997.5 \pm 79.28$  and  $940.1 \pm 45.39$  days respectively for premenopausal and postmenopausal women (Figure 3).

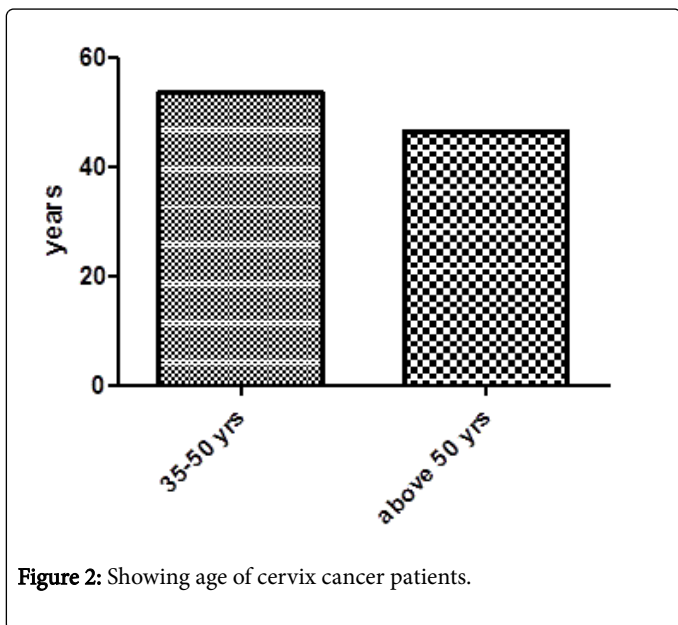


Figure 2: Showing age of cervix cancer patients.

The mean duration for overall survival for all cases evaluated was  $957.4 \pm 39.49$  days. The mean duration for survival of stages I,II,III,IVA was  $1186 \pm 281.8$ ,  $960 \pm 85.04$ ,  $945.1 \pm 45.66$  and  $765 \pm 181.5$  days respectively (Figure 4). This showed that patients who presented in early stage had a better survival.

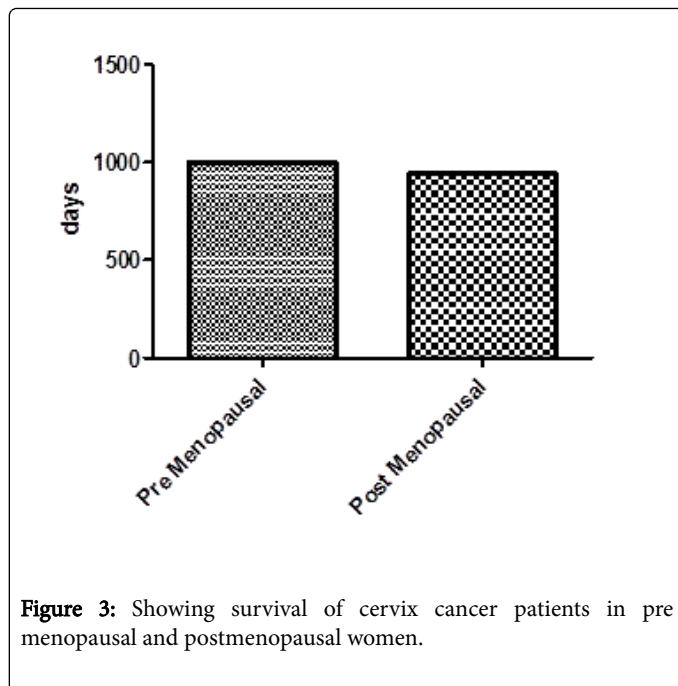


Figure 3: Showing survival of cervix cancer patients in premenopausal and postmenopausal women.

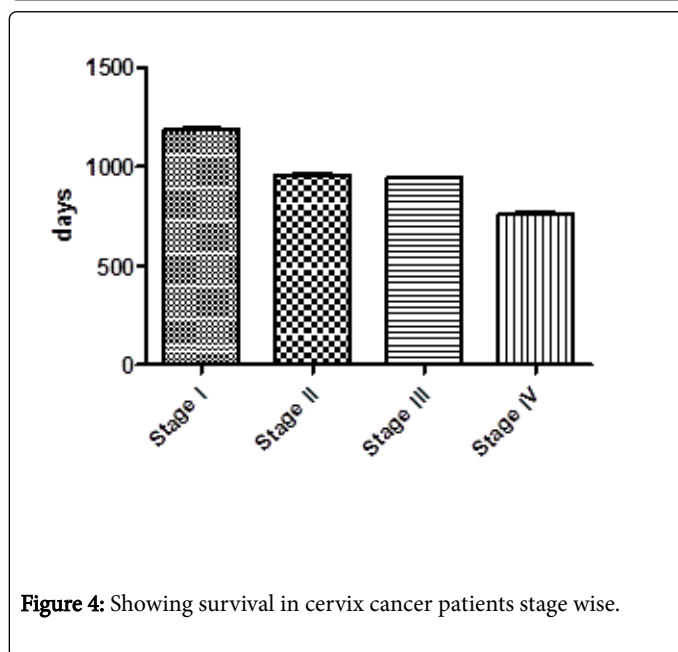


Figure 4: Showing survival in cervix cancer patients stage wise.

Survival was analysed between patients having squamous cell carcinoma and adenocarcinoma of cervix. 89.96% of patients had squamous cell carcinoma and their survival was  $970 \pm 42.89$  days. 10.04% of the patients had adenocarcinoma of cervix had survival of  $669.5 \pm 120$  days (Figure 5). This study also showed that prognosis for squamous cell carcinoma was far better than adenocarcinoma of cervix.

Overall treatment time, that is, the duration from the start of external beam radiotherapy to the end of intracavitary radiotherapy, for all the patients calculated, was  $72.95 \pm 0.77$  days. In the study the overall treatment time was  $72.95 \pm 0.77$  days with an overall survival of  $957.4 \pm 39.49$  days with a significant P value of less than 0.0001. A total

of 13.54% of the patients who came for follow up had either local recurrence or distant failures.

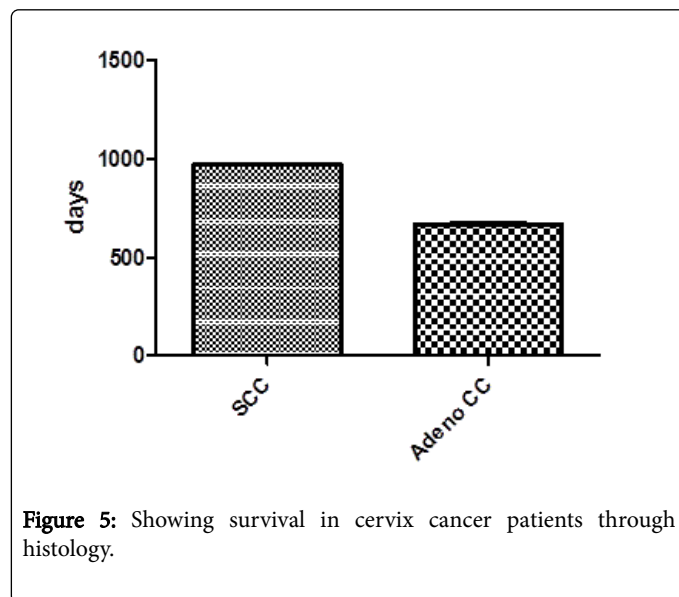


Figure 5: Showing survival in cervix cancer patients through histology.

## Discussion

The various registries of developing countries show that cervical cancer develops in 80 to 90% cases in ages more than 35 years [10]. Study done by Beckley et al reported an average age of 48 years for occurrence of cervical cancer [11]. In a study done in South India by Sridevi et al, peak age of occurrence was between 55 and 59 years [12]. In our study the incidence for cervical cancer patients ranged from 36 to 70 years, the mean age being 50.38 years with a median age of 50 years. This was less than that reported in other parts of the country. This shows that there is an alarming need for screening in the early ages as compared to other parts of the world.

The study conducted by Sankanarayanan et al in Kerala, India showed that modal presentation of cervical cancer was in stage IIIB [13]. Study conducted in Nigeria showed 72.3% were in advanced stages at presentation [14]. In our study 71.65% of the patients were of stage II followed by 22.83% of stage III. This result showed the enormous burden of late presentation of cervical cancer at advanced stages with only option of radiotherapy with or without concurrent chemotherapy.

Survival study conducted by Muhamad also showed that women in less than 45 years old had a better survival compared to older than 45 years [15]. In our study also Survival of age group between 35 to 50 years was slightly more than patients of age more than 50 years. Perimenopausal women are at higher risk for cervical cancer and the peak incidence occurs between ages of 50 to 52 years [16]. In our study majority of patients were postmenopausal with a lesser survival. Relatively inferior survival in postmenopausal women could be due to increasing age and various comorbid conditions.

The two most common type of histology for cervical cancer reported is squamous cell carcinoma and adenocarcinoma. Study done by Brinton et al showed incidence of squamous cell carcinoma and adenocarcinoma is 74.4% and 15.5% respectively [17]. The risk of death increases for adenocarcinoma of cervix compared to squamous cell carcinoma [18]. Survival rates reported has been higher for

squamous cell carcinoma versus adenocarcinoma [19]. In our study also survival for squamous cell carcinoma had been far better than adenocarcinoma cervix.

Radiotherapy is an effective treatment modality for all stages of Cancer Cervix and is the main modality used in developing countries [20]. According to Viladiu et al clinical stage was the only independent prognostic factor for cervical cancer [21]. Cervical cancer patients diagnosed with stage IA has 100% chance of survival as compared to stage IVB who had a chance of survival of about 20% [22, 23]. According to caio et al, 5 year survival for stage I, II, III reported was 74%, 56%, 33% respectively [24]. The overall 5 years survival after radiotherapy for cervical cancer was 68.2% for all stages and being 86.3, 81.1, 73.0, 50.3, 47.8 and 7.8% for stages IB, IIA, IIB, IIIA, IIIB and IVA respectively as reported by Lorvidhyal [25]. Another study by Benedet showed survival of 95%, 80%, 63%, 36% and 15% respectively for stages IA, IB, II, III and IV respectively [26]. Study done by Aria et al showed that survival was 88.1% for stage IB, 76.9% for stage II, 67% for stage IIB, 52.2% for stage IIIB, 24.1% for stage IVA and 13.3% for stage IVB of the disease [27]. According to Kaverappa five year survival rate for cervical cancer was found to be 48.1% at a tertiary hospital in India [28]. The prognosis of cervix cancer in elderly was reported to be inferior in comparison to younger patients [29]. In our study survival analysed for stage I, II, III and IV A was  $1186 \pm 281.8$ ,  $960 \pm 85.04$ ,  $945.1 \pm 45.66$  and  $765 \pm 181.5$  days respectively. Our study of decreasing survival with increasing stage matched with other studies.

According to Fyles Overall Treatment Time (OTT) is one of most important prognostic factor [30]. Overall treatment time had a greater impact on local control as study done by Grinsky showed that there was an increase in local recurrence by 5 to 10% when overall treatment time exceeded more than 10 weeks [31]. Study done by Lanciano also suggested that overall treatment time less than or equal to 55 days was associated with longer survival [32]. A recent study conducted in France by Krebs et al showed that overall treatment duration is as important as dose to the high risk clinical target volume to achieve complete response in cervical cancer [33].

In our study the overall treatment time was  $72.95 \pm 0.77$  days with an overall survival of  $957.4 \pm 39.49$  days with a significant P value of less than .0001. This was certainly high than the other reported studies. The longer duration of overall treatment time was attributable to many factors including the policy of performing ICRT only after 5 weeks of EBRT, poor compliance of the patients, long waiting in brachytherapy unit and many others.

## Conclusion

To conclude in our group of patients the mean survival for patients in all stages was  $957.4 \pm 39.49$  days which was more than 2 years 7 months. Also our study showed that survival was better in patients of age group 35 to 50 years with those of them having squamous cell carcinoma. It also showed that premenopausal women had better survival than postmenopausal women. Squamous cell carcinoma of cervix has shown better survival than adenocarcinoma variant. Survival of cervical cancer was very much dependent on the age, stage and histology of cervical cancer.

## References

1. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB (2005) Cancer incidence in five continents. Lyon: IARC Press.

2. Aswathy S, Quereshi MA, Kurian B, Leelamoni K (2012) Cervical cancer screening: Current knowledge & practice among women in a rural population of Kerala, India. *Indian J Med Res* 136: 205-210.
3. Carmo CC, Luiz RR (2011) Survival of a cohort of women with cervical cancer diagnosed in a Brazilian cancer center. *Rev Saúde Pública* 45: 661-667.
4. Pardo C, Cendales R (2009) Supervivencia de pacientes con cáncer de cuellouterinotratadas en el Instituto Nacional de Cancerología. *Biomédica (Bogotá)* 29: 437-447.
5. Coker A, Du X, Fang S, Eggleston K (2006) Socioeconomic status and cervical cancer survival among older women: findings from the SEER-Medicare linked data cohorts. *Gynecol Oncol* 102: 278-284.
6. Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S (2007) Human papillomavirus and cervical cancer. *Lancet* 370: 890-907.
7. Chichareon S, Herrero R, Muñoz N, Bosch FX, Jacobs MV, et al. (1998) Risk Factors for Cervical Cancer in Thailand: a Case-Control Study. *J Natl Cancer Inst* 90: 50-57.
8. Mileshkin L, Paramanathan A, Kondalsamy-Chennakesavan S, Bernshaw D, Khaw P, et al. (2014) Smokers with cervix cancer have more uterine corpus invasive disease and an increased risk of recurrence after treatment with chemoradiation. *Int J Gynecol Cancer* 24:1286-1291.
9. Tan LT, Orton CJ, Blake PR, Jones B (2004) Gynaecological brachytherapy: A 1 day seminar organized by the British Institute of Radiology Brachytherapy Working Party. *Br Journal of radiology* 77:1-2.
10. Morley GW, Lindeau SM (1976) Pelvic exenterative therapy for Gynecologic malignancy an analysis of 70 cases. *Cancer* 38(1):581-586.
11. Byckley CH, Beard CS, Fox H (1998) Pathologic prognostic indicators in cervical cancer with particular reference to age under 40 years. *Br J of Obstetrics and Gynecology* 95:47-56.
12. Sreedevi A, Javed R and Dinesh A (2015) Epidemiology of cervical cancer with special focus on India. *International Journal of Women's Health* 7: 405-414.
13. Sankaranarayananl, Krishnan Nair M, Jayaprakash PG, Stanley G, Varghese C, et al. (1995) Cervical cancer in Kerala: a hospital registry-based study on survival and prognostic factors. *British Journal of Cancer* 72: 1039-1042.
14. Jonah Musa, Joseph Nankat, Chad J Achenbach, Iornum H Shambe, Babafemi O Taiwo, et al. (2016) Cervical cancer survival in a resource-limited setting-North Central Nigeria. *Infectious Agents and Cancer* 11:15.
15. Muhama Na, Muhammad AK, Mohd Y, Mohamed AN, Mohammed FB, et al. (2015) *Asian Pac J Cancer Prev* 16: 3067-3072.
16. Cheung FY, Mang OW, Law SC (2011) A population-based analysis of incidence, mortality, and stage-specific survival of cervical cancer patients in Hong Kong: 1997-2006. *Hong Kong Med J* 17: 89-95.
17. Brinton LA, Tashima KT, Lehman HE, et al. (1987) Epidemiology of cervical cancer by cell type. *Cancer Res* 47:1706-1711.
18. Burger RA, Monk BJ, Kurosaki T, Anton-Culver H, Vasilev SA, et al. (1996) Human papillomavirus type 18: association with poor prognosis in early stage cervical cancer. *J Natl Cancer Inst* 88: 1361-1368.
19. Chen T, Jansen L, Gondos A, et al. (2012) Survival of cervical cancer patients in Germany in the early 21st century: a period analysis by age, histology, and stage. *Acta Oncol* 51: 915-921.
20. Saibishkumar EP, Patel FD, Sharma SC (2006) Evaluation of late toxicities of patients with carcinoma of the cervix treated with radical radiotherapy: An audit from India. *Clin Oncol (R Coll Radiol)* 18: 30-37.
21. Viladiu P, Bosch FX, Castellsague X, Muñoz N, Escriba JM, et al. (1997) Human papillomavirus DNA and antibodies to human papilloviruses 16 E2, L2 and E7 peptides as predictors of survival in patients with squamous cell cervical cancer. *J Clin Oncol* 15: 610-619.
22. Kyrgiou M, Shafi MI (2010) Invasive cancer of the cervix. *Obstetrics Gynaecol Reproductive Med* 20: 147-154.
23. Razak NA, Mn K, Zubairi YZ, et al. (2013) Estimating the five year survival of cervical cancer patients treated in hospital Universiti Sains Malaysia. *Asian Pac J Cancer Prev* 14: 825-828.
24. Coia L, Won M, Lanciano R, Marcial VA, Martz K, Hanks G (1990) The patterns of care outcome study for cancer of the uterine cervix. Results of the second national practice survey. *Cancer* 66: 241-256.
25. Lorvidhaya V, Tonusin A, Changwiwit W, et al. (2000) High dose-rate afterloading brachytherapy in carcinoma of the cervix: an experience of 1992 patients. *Int J Radiation Oncol Biol Phys* 46: 1185-1191.
26. Benedet J (2001) Annual report on the treatment of GYN CA. *J Epidemiol Biostat*.
27. Arai T, Nakano T, Morita S, Sakashita K, Nakamura YK, et al. (1992) High-dose-rate remote afterloading intracavitary radiation therapy for cancer of the uterine cervix. A 20-year experience. *Cancer* 69: 175-180.
28. Vishma B Kaverappa, Prakash Boralingaiah, Praveen Kulkarni, Renuka Manjunath (2015) Determinants of Survival among Patients with Cervical Cancer: A Hospital Based Study. *Natl J Community Med* 6: 137-142.
29. Ming Yin Lin, Srinivas Kondalsamy-Chennakesavan, David Bernshaw, Pearly Khaw, Kailash Narayan (2016) Carcinoma of the cervix in elderly patients treated with radiotherapy: patterns of care and treatment outcomes. *J Gynecol Oncol* 27: 59.
30. Fyles AW, Pintilie M (1995) Prognostic factors in patients treated cervix cancer treated by radiation therapy: results of multiple regression analysis. *Radiotherapy Oncol* 35: 107-117.
31. Girinsky T, Rey A, Roche B, Haie C, Gerbaulet A, et al. (1993) Overall treatment time in advanced cervical carcinomas: a critical parameter in treatment outcome. *Int J Radiation Oncology Biol Phys* 27: 1051-1056.
32. Lanciano RM, Won M, Coia LR (1991) Pretreatment and treatment factors associated with improved outcome in squamous cell carcinoma of the uterine cervix: A final report of the 1973 and 1978 patterns of care studies. *Int J Radiat Oncol Biol Phys* 20: 667-676.
33. Krebs L, Maillard S, Gaillot-Petit N, Ortholan C, Nguyen TD (2015) Total radiation dose and overall treatment time are predictive for tumor sterilization in cervical carcinoma treated with chemoradiation and pulsed-dose-rate brachytherapy. *Brachytherapy* 14: 16-22.