

# Cervical Cancer Treatment in Aging Women

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## 1. Introduction

In Japan, the elderly population has been rapidly increasing, and the “aging society” is currently considered one of the nation’s most important social concerns. According to statements by the Ministry of Health, Labour, and Welfare, the average life spans of men and women in 2008 were 79 and 86 years, respectively, and that of women in Japan is the longest in the world (Ministry of Health, Labour, and Welfare, 2009). The percentage of the elderly population in Japan will continue to increase. With the growing aging society, the number of elderly patients with various malignancies has been increasing. However, the rate of cancer in younger patients has also been increasing, due to changes in lifestyles, such as the increased popularity of Western food, viral infections, and genetic factors. In Japan, malignant neoplasms demonstrate the highest mortality rate, surpassing cerebrovascular and heart diseases since 1981, and lung cancer has demonstrated the highest mortality rate among every malignancy in both men and women.

Cervical cancer affects a wide age demographic, but, recently, the prevalence of disease among young women has been emphasized. It is well known that the most common cause of cervical cancer is human papilloma virus (HPV). Sexual relationships in younger women with little knowledge of sexually transmitted diseases appear to be an important factor contributing to the prevalence of HPV infection. In Japan, the most commonly afflicted age group is women in their late 30s to early 40s. Cervical cancer is one of the most common forms of cancer women aged  $\leq 39$  years old. The prevalence rate decreases for women aged 50 to 60 years and increases again for women in their 70s. As a result of the aging society and re-increase of prevalence rate, the number of elderly patients with cervical cancer has been increasing in Japan. The number of elderly patients with cervical cancer in the Western countries with aging societies has also been increasing as in Japan. We should remember that a 77-year-old cervical cancer patient, for example, may live for 10 to 20 additional years if the disease is cured and that these elderly patients should be treated with radical modalities similar to those used on young patients to achieve successful outcome. However, treatment modalities should be selected carefully because of the high likelihood of toxicity from the treatment and concurrent medical problems, such as hypertension, diabetes mellitus, dementia, cerebral infarction, and other cancers. In the daily clinical setting, the opportunities for treating elderly patients with several concurrent medical problems are increasing.

The basic treatment modality for cervical cancer is a surgical approach or radiotherapy (RT). In general, surgery is performed for patients with early-stage cervical cancers. RT can be performed for the patients with early- to advanced-stage cervical cancer. Additionally, in the previous reports, the treatment results of surgery and RT for early-stage cervical cancer were similar (Landoni et al., 1997; Perez et al., 1995 and Yamashita et al., 2005). Furthermore, RT appears to be a less invasive modality compared to surgery. These facts indicate that RT is a more appropriate treatment for the elderly patient population.

The aim of this chapter is to discuss the treatment modalities for elderly patients with cervical cancer with a focus on RT based on the knowledge from our experience and previous reports.

## **2. Details of a standard RT method, including recommendations for elderly patients with cervical cancer and a review of treatment outcomes**

Selecting a treatment modality for elderly patients, cautious evaluation of their general condition, clinical staging, and concurrent medical problems are important because they usually do not tolerate treatment-related toxicity as well as do young patients. Inadequate treatment may result in lethal toxicity. Generally, RT is thought to be one of the most suitable modalities for preserving quality of life, and, therefore, RT is important for elderly patients. In this section, the general knowledge of clinical manifestations and pretreatment evaluation of elderly patients are described. Subsequently, the details of a standard RT method for cervical cancer, including recommendations for elderly patients, are illustrated, and the treatment outcomes of RT for elderly patients with cervical cancer are discussed.

### **2.1 Clinical manifestations and pretreatment evaluation**

The most frequent and important clinical manifestation of cervical cancer is irregular vaginal bleeding. Other important clinical manifestations include bleeding during sexual activity, increase of vaginal discharge and lower-back pain. For advanced disease, the bleeding sometimes becomes severe, and blood transfusions are usually performed. Severe bleeding may have lethal results in elderly patients.

Clinical staging is generally performed according to the International Federation of Gynecology and Obstetrics (FIGO) stages (Creasman, 1995). However, thoracic to pelvic computed tomography (CT) or pelvic magnet resonance imaging (MRI) must be performed in both elderly and younger patients. Additionally, positron emission tomography (PET) scans should also be performed, if possible. These imaging procedures are useful for clinical staging and are important for the determination of the treatment modality. Similarly, pretreatment evaluation, including concurrent medical problems and performance status, is also important because elderly patients usually do not tolerate treatment-related toxicity as well as do younger patients. Using these methods, adequate treatment modalities for elderly patients can be determined.

### **2.2 Standard RT method for cervical cancer, including recommendations for elderly patients**

According to the Clinical Practice Guideline in Oncology from the National Comprehensive Cancer Network (NCCN) guidelines (National Comprehensive Cancer Network, 2011), RT

is recognized to be important in the definitive treatment. For FIGO stage IA2 disease, radical hysterectomy (RH) + pelvic lymph node dissection (PLND) ± para-aortic lymph node sampling, or intracavitary brachytherapy (ICBT) ± pelvic RT, or radical trachelectomy + PLND ± para-aortic lymph node sampling is recommended. In addition, for FIGO stage IB1 or IIA1, RH + PLND ± para-aortic lymph node sampling, or pelvic RT + ICBT, or radical trachelectomy for tumors ≤ 2 cm (stage 1B1) + PLND ± para-aortic lymph node sampling is recommended. These recommendations indicate that RT can be used in early-stage diseases, and its importance increases in advanced-stage diseases. In other words, RT can be used to treat cervical cancer at any stage, and it is the most important treatment modality for elderly patients.

External beam radiotherapy (EBRT) combined with ICBT is the standard RT method for cervical cancer. For EBRT, patients were initially treated with whole-pelvic RT using a box field. The gross tumor, whole uterus, pelvic lymph nodes, parametria and uterosacral ligaments must be included in the RT field. Additionally, a sufficient vaginal margin from the gross disease (at least 3 cm) is necessary. In X-ray films, the superior limit is the upper border of the 5<sup>th</sup> lumbar, and the inferior limit is the lower border of the obturator foramen for the anterior/posterior RT field. For the lateral RT field, the anterior limit is approximately 0.5 cm behind the pubic joint, and the posterior limit should involve the entire sacrum. In Japan, a centrally shielded field using an anterior/posterior opposed field is applied just before the starting ICBT subsequent to whole-pelvic RT to reduce the doses for organs at risk, especially the rectum and bladder. The daily fraction size of EBRT is approximately 1.8 to 2.0 Gy in general. The total dose of pelvic RT is 45.0 to 50.4 Gy. Although standard EBRT for cervical cancer is performed using a 3D technique, while a new RT method, which is known as intensity modulated radiotherapy (IMRT), has been expanding in many institutions. IMRT achieves the dose reduction of organs at risk, such as the rectum, bladder, colon, and small intestine, in the pelvic RT. Dose reduction for these organs will provide certain benefits, especially for elderly patients.

ICBT using a distinctive dose prescription point known as "Point A" is performed to boost the primary tumor and is an indispensable procedure in the RT of cervical cancer. Traditionally, low-dose rate ICBT (LDR-ICBT) was usually used, but high-dose rate ICBT (HDR-ICBT) using a 192-iridium remote afterloading system has become favored over LDR-ICBT. In Japan, most patients are treated with HDR-ICBT, and it is performed 3 to 5 times at 1-week intervals during EBRT. Generally, the single fraction size of HDR-ICBT ranges from 5.0 to 6.0 Gy, and the total dose is 15.0 to 29.0 Gy. Patients with higher stage diseases are usually treated with higher doses of whole-pelvic RT and lower doses of ICBT. Patients with lower-stage diseases are usually treated with higher doses of ICBT and lower doses of whole-pelvic RT. It is also important to reduce the doses for organs at risk in ICBT as well as EBRT. When performing ICBT, we should consider that toxicity from overdose to the rectum and bladder may lead to lethal results for elderly patients with cervical cancer. The doses for the rectum and bladder are evaluated according to the recommendation of ICRU Report 38 in most institutions (International Commission on Radiation Units and Measurements, 1985); however, these recommendations are based on the use of 2D treatment planning using X-ray films. Recently, 3D treatment planning systems for brachytherapy using CT or MRI, which are known as image-guided brachytherapy (IGBT), have been gradually expanding similarly to IMRT. Using this technique, the doses for the rectum and bladder are calculated more accurately compared to past treatment methods,

and a more adequate dose distribution for the gross tumor will be achieved. In the near future, IGBT will be the preferred method in the treatment planning of brachytherapy. In the treatment of elderly patients, RT induced toxicity must be reduced as much as possible. The standard definitive RT methods and doses for cervical cancer in Japan according to stage (tumor size) are described in Table 1 (Japan Society of Obstetrics and Gynecology, The Japanese Society of Pathology, Japan Radiological Society, 1997).

stage (tumor size)	EBRT (Gy)		HDR-ICBT (Gy / fractions)
	whole pelvis	centrally-shielded	
I	0	45-50	29 / 5
II (small)	0	45-50	29 / 5
II (large)	20	30	23 / 4
III (small to middle)	20-30	20-30	23 / 4
III (large)	30-40	20-25	15-20 / 3-4
IVA	30-50	10-20	15-20 / 3-4

EBRT: External beam radiotherapy, HDR-ICBT: High dose rate intracavitary brachytherapy

Table 1. Standard definitive RT methods and doses according to stage (tumor size)

A boost to the primary tumor by EBRT is an alternative method for elderly patients because they are usually in poor condition, due to concomitant medical problems, and these patients may not be tolerant of ICBT. To reduce the irradiated volume, retreatment planning based on newly obtained CT scans should be performed just before the start of the boost. In our institution, the most commonly used dose is 10.0 Gy in 5 fractions. ICBT alone for small tumors is also a treatment choice for elderly patients who cannot continue long-term hospitalization because of dementia or other mental problems. Additionally, pelvic RT with smaller fields, reducing the dose of ICBT, and other efforts should be performed to avoid severe toxicity for elderly patients with poor performance statuses.

A boost to the gross lymph node involvement on CT or MRI is often performed because the lymph node usually cannot be controlled by 50 Gy of pelvic RT. Although the boost to the lymph node involvement is important for cure, it may be too aggressive for elderly patients. Therefore, indication should be determined with caution. Patients with poor performance statuses from the beginning of RT, patients who experienced severe acute toxicity, or patients with multiple lymph node involvement (3 or more) should be excluded. Similar to the boost to the primary tumor by EBRT, retreatment planning based on newly obtained CT should be performed just before the start of the boost. In our institution, the most commonly used dose is 10.0 Gy in 5 fractions. Using IMRT will provide higher safety for elderly patients when the boost to the primary tumor or lymph node involvement is performed.

Para-aortic lymph node involvement is an evidence of advanced disease. For these patients, extended-field RT including the entire pelvis and the para-aortic region is sometimes performed. Extended-field RT is an aggressive modality for elderly patients. Treatment delay will often occur, and some patients cannot complete RT. Moreover, patients with advanced disease usually demonstrate poor performance status. Therefore, extended-field RT does not seem to be suitable for elderly patients. Palliative RT should be recommended

for elderly patients with para-aortic lymph node involvement, while excluding patients in quite good condition.

### 2.3 Treatment outcomes of definitive RT for elderly patients with cervical cancer

Several reports have examined the treatment results of RT for elderly patients with cervical cancer. As for Japanese papers, Sakurai et al. retrospectively evaluated 380 patients with cervical cancer treated with definitive RT between 1970 and 1994 (Sakurai et al., 2000). Of the 380 patients, 215 were younger than 70 years, 124 were 70 to 79 years, and 41 were 80 years or older. All of the patients were treated with EBRT combined with LDR-ICBT. They reported that the 5-year overall survival (OS) rate in the youngest (younger than 70 years), intermediate (70 to 79 years), and oldest (80 years or older) groups were 58%, 50%, and 33%, respectively. The 5-year OS rate in the oldest group was significantly worse than that of the youngest group. They also reported that the 5-year cause-specific survival (CSS) rate in the youngest, intermediate, and oldest groups were 68%, 70%, and 65%, respectively. The CSS rates were not significantly different among the 3 groups. For the chronic complications, Grade 3 or 4 occurred in 6.5% of the youngest, 11.3% of the intermediate, and 7.3% of the oldest group. No significant differences were observed in those complications among the 3 groups. They concluded that EBRT combined with LDR-BT proved to be highly effective and safe for elderly patients with cervical cancer. Ikushima et al. retrospectively evaluated 727 patients treated with definitive RT between 1970 and 1994 (Ikushima et al., 2007). In this report, 727 patients were also divided into 3 groups. Patients aged  $\leq 64$  years ( $n = 337$ ) was defined as the younger group (YG), patients aged 65 – 74 years ( $n = 258$ ) were defined as the young-old group (YOG), and patients aged  $\geq 75$  years ( $n = 132$ ) composed the older group (OG). EBRT combined with LDR-ICBT was the basic treatment. However, 16 of 337 patients in the YG, 7 of 258 in the YOG, and 10 of 122 in the OG were not treated with LDR-ICBT. The 5- and 10-year OS rates were 59% and 49% in the YG, 68% and 51% in the YOG, and 49% and 30% in the OG, respectively. The differences in the 5- and 10-year OS rates between the OG and other groups were significant. The 5- and 10-year disease-specific survival (DSS) rates were 60% and 52.5% in the YG, 75.7% and 67.8% in the YOG, and 65.9% and 56.7% in the OG, respectively. In this study, the 5- and 10-year DSS rates in the YG were worse compared to the other groups, and the differences between the YG and the YOG were significant. Grade 2-4 late radiation morbidity in the bladder and/or rectum occurred in 22% of the YG, 31% of the YOG, and 8% of the OG. Grade 3-4 morbidity did not occur in the OG. They concluded that age was not a significant prognostic factor, and, in the management of cervical cancer, advanced age was not a contraindication to radical RT. We also retrospectively evaluated 40 patients aged  $\geq 75$  years who were treated with RT between 2000 and 2009 (9 were treated between 2000 and 2005, and 31 were treated between 2006 and 2009). In our study, 35 patients were treated with definitive RT, and 5 were treated with surgery + adjuvant RT (Yoshida et al., 2011). Among the 35 patients treated with definitive RT, 31 were treated with EBRT combined with HDR-ICBT. Of the remaining 4 patients, 3 were treated with EBRT alone and 1 with HDR-ICBT alone because of their medical condition. Of the initial 40 patients, 38 completed the treatment as planned, 1 completed with a delay, due to concomitant heart disease, and 1 could not complete the treatment because of acute toxicity. The 3-year OS and DSS rates for all of the patients were 58% and 80%, respectively, with a median follow-up of 20 months. Both acute and late toxicity were evaluated in our study. Grade 3 acute toxicity occurred in 5 patients. Of the 3

patients, 3 were treated with surgery + adjuvant RT. Grade 4 toxicity did not occur. Grade 3 late toxicity occurred in 2 patients. Of the two patients, one was treated with surgery + adjuvant RT, and the other was treated with BERT + HCR-ICBT with concurrent chemotherapy. Although the median follow-up was shorter, and a smaller number of patients were evaluated, our results were consistent with 2 large Japanese studies. We concluded that definitive RT for elderly patients was generally effective and safe, but aggressive treatment, such as surgery + adjuvant RT, concurrent chemoradiation, or a combination of these modalities, should be performed with caution.

Studies from other countries have also reported results regarding elderly patients with cervical cancer treated with RT. Mitchell et al. retrospectively analyzed 398 patients treated with RT between 1975 and 1993. Patients were divided into nonelderly (ages 35-69, n = 338) and elderly (ages  $\geq 70$ , n = 60) groups (Mitchell et al., 1998). The basic RT method was a combination of EBRT and LDR-ICBT. However, 12.9% of the nonelderly group and 31.7% of the elderly group did not receive RT. The 5-year OS rates were 58.0% in the nonelderly group and 46.4% in the elderly group. The difference in the OS rate between the 2 groups was significant. However, the 5-year CSS rates were 76.3% in the nonelderly group and 84.1% in the elderly group. Unlike the OS rate, the CSS rate in the elderly group was better than in the nonelderly group, but this difference was not significant. The frequency and severity of acute and chronic toxicity were similar in both groups, and they concluded that definitive RT was effective and also well tolerated in elderly cervical cancer patients. Chen et al. described 295 patients treated with definitive RT between 1992 and 1997 and focused on HDR-ICBT (Chen et al., 2003). Patients were divided into 2 groups. Patients under 70 years of age (n = 179) were defined as a younger group, and patients aged 70 years or older (n = 79) were included in an older group. They used whole-pelvic RT with a total dose of 45-50 Gy in 20-25 fractions over 4-5 weeks. A boost for patients with FIGO IIB-IVA bilateral parametrial disease was performed up to 54-58 Gy using central shielding. After the completion of whole-pelvic RT, HDR-ICBT was performed at 1-week intervals. The standard dose to Point A for three insertions (before July 1995) was 7.2 Gy or 6.0 Gy (after July 1995). The authors noted that the Point A dose was decreased to 5.0 Gy for all 79 patients in the older group. Survival was calculated according to age and clinical stage. The 5-year respective OS for the older and younger groups were 82% and 85% for stage IB, 65% and 65% for IIA, 61% and 71% for 2 IIB, and 35% and 59% for 3 IIIA-B, respectively. No significant differences were observed. The respective 5-year CSS rates for the older and younger groups were 100% and 95% for IB, 85% and 75% for IIA, 78% and 72% for IIB, and 42% and 61% for IIIA-B, respectively. No significant differences were observed. As for the complications, only 3 patients developed acute Grade 3-4 gastrointestinal complications (2 in the older and 1 in the younger group). Twelve (15%) patients in the older group and 14 (7.8%) in the younger group developed late Grade 3-4 rectal complications, while 7 (8.9%) patients in the older group and 10 (5.6%) patients in the younger group developed Grade 3-4 small bowel complications. No significant difference was observed between the 2 groups for Grade 3-4 complications. The authors concluded that a combination of EBRT and HDR-ICBT was effective and tolerable for elderly patients.

The results in these reports indicated that there were no significant differences in the CSS (DSS) rates between the elderly and younger patients. Although several papers noted that the OS rate in elderly patients was significantly worse than the younger patients, this result

was due to the increase of death from other causes in the elderly population and was expected. Toxicity due to RT was similar in both elderly and younger patients in all of the reports. Therefore, definitive RT, especially a combination of EBRT and ICBT, was equally effective for elderly patients and younger patients. Using IMRT, IGBT, or both, further reduction of treatment-related toxicity will be achieved with excellent treatment outcomes. In the near future, a combination of IMRT and IGBT will be the standard method of definitive RT for elderly patients with cervical cancer.

### 3. Surgical approaches for elderly patients

A surgical approach for elderly patients with cervical cancer is controversial. Conization of the cervix for FIGO stage 0 cancer is well tolerable, even for elderly patients, but the standard surgical approach, RH and PLND, appears to be invasive. Wright et al. retrospectively analyzed 1582 patients with cervical cancer who were treated between 1986 and 2003 (Wright et al., 2005). Of the 1582 patients, 1385 were aged < 70 years, and 197 were aged  $\geq$  70 years. Surgery (including RH, modified RH, extrafascial hysterectomy, or trachelectomy) was performed for 753 of 1385 (54.4%) patients aged < 70 years and was performed for 32 of 197 (16.2%) patients aged  $\geq$  70 years. However, RT or chemoradiation (CRT) was performed for 605 of 1385 (43.7%) patients aged < 70 years and was performed for 156 of 197 (79.1%) patients aged  $\geq$  70 years. They stressed that younger patients were more likely to undergo surgery, and older patients were more likely to receive RT. There are several reports about RH for cervical cancer concerning age. Fuchtnner et al. (1992) compared 45 women older than 65 years treated with RH and 90 women less than 65 years treated similarly (Fuchtnner et al., 1992). Although transfusions were required more frequently in the elderly patients, there were no significant differences in survival or complications. They concluded that age alone should not be a contraindication for RH in elderly patients with cervical cancer. Geisler et al. examined 62 patients aged over 65 years who underwent RH and a lymphadenectomy between 1965 and 1998 (Geisler et al., 2001). These patients were matched with 124 patients aged 50 years or younger who underwent the same procedure. Although the period of the postoperative hospital stay was longer in the elderly group than the younger group, there were no significant differences in the percentages of intraoperative and postoperative complications. They concluded that radical hysterectomy is a safe surgical procedure in a select population of patients aged 65 years or over. Mousavi et al. retrospectively evaluated 22 patients aged 60 years and above who underwent a Wertheim RH between 1999 and 2005, comparing 128 matched cases under 60 years who underwent the same procedure during the same period (Mousavi et al., 2008). There were no operative mortalities in either group, and there was no significant difference in morbidity between the 2 groups. The mean postoperative hospital stay was significantly longer in the older patients. They concluded that Wertheim RH is a safe surgical procedure in the selected population of patients aged 60 years and older. From the results of these reports about RH, the authors emphasized that it was a safe treatment modality for elderly patients. However, they defined "elderly" as "60 years and above" or "over 65 years." On the other hand, in the reports about RT, "elderly" was defined as "over 70 years" or "75 years or older." In recent years, "elderly" generally includes patients aged 75 years or older or at least over 70 years. Therefore, patients defined as elderly in reports about RH were considered to be "middle aged." Therefore, whether RH is safe for elderly patients aged "over 70 years" or "75 years or older" remains unclear.

Patients treated with RH + PLND with pathological risk factors, such as lymph node metastasis, lymphatic, vascular, or deep stromal invasion, should receive postoperative adjuvant RT. RH + PLND and adjuvant RT is considered an aggressive treatment and, generally, treatment-related toxicities, such as adhesive intestinal obstruction, or lymphatic edema of the lower extremities, increases compared to surgery or RT alone. Kashima et al. evaluated 149 patients with cervical cancer treated with RH or combined with postoperative RT between 1990 and 2004 (Kashima et al., 2010). Of the 149 patients, 41 were over 60 years, and 105 were under 59 years. The complications were significantly higher in the elderly patients and especially in those treated with RH combined with postoperative RT. In our study, 5 patients aged  $\geq 75$  years were treated with surgery (RH + PLND) and adjuvant RT. Three of the 5 patients experienced Grade 3 acute toxicity and 1 of the 5 patients experienced Grade 3 late toxicity. The results of these reports indicated that surgery and adjuvant RT were not safe for elderly patients. If adjuvant RT is necessary for elderly patients, IMRT may be used to limit severe toxicity.

Overall, the standard surgical approach RH + PLND is generally safe for patients aged over 60 or 65 years. However, the safety of RH + PLND for patients aged over 70 or 75 years is still unclear. Surgery and adjuvant RT must be performed with careful evaluation of pretreatment clinical staging, concurrent medical problems, and performance status for these age groups because severe life-threatening treatment-related toxicity may occur. More large-scale studies should be performed to confirm the safety of surgical approaches, including adjuvant RT for elderly patients.

#### **4. Concurrent CRT for elderly patients**

Concurrent CRT for elderly patients should also be discussed. Generally, in the treatment of cervical cancer, concurrent CRT is recommended, especially for locally advanced disease (Eifel et al., 2004; Rose et al, 1999; Whitney et al, 1999 and Pearcey et al., 2002). Weekly cisplatin (CDDP) is the most frequently used regimen. Concurrent CRT is also regarded as important for elderly patients because stage III-IVA disease usually cannot be cured by definitive RT alone. Therefore, CRT should be considered if the elderly patient is in good condition. Goodheart et al. retrospectively evaluated 96 patients treated with definitive RT between 1997 and 2001 (Goodheart et al., 2008). In their report, patients were divided into 2 groups: nonelderly ( $< 65$ ,  $n = 69$ ) and elderly ( $\geq 65$ ,  $n = 27$ ). Chemotherapy administration was considered when the performance status and laboratory values were acceptable. Most of the patients were administered weekly CDDP. In the nonelderly group, 54 of 78 (78%) patients were treated with CRT, and, in the elderly group, 15 of 27 (56%) patients were treated with CRT. The 5-year CSS rates in the CRT and RT group were 68.5% and 49.7%, respectively. The 5-year CSS rates in the nonelderly and elderly groups were 61.6% and 70.8%, respectively. Multivariate analyses showed a survival advantage for the administration of chemotherapy in addition to RT, and complication rates between the 2 groups were similar. They concluded that CRT was associated with improved survival in elderly patients who had adequate performance status with no excess treatment-related morbidity when compared to younger patients. Kunos et al. also examined 335 patients with locally advanced cervical cancer treated with CRT using weekly CDDP (Kunos et al., 2009). Patients were also divided into 2 groups: age  $< 55$  years ( $n = 232$ ) and age  $\geq 55$  years ( $n = 103$ ). In their report, the survival of patients aged 55 or older was similar to that of the younger patients. The severity and frequency of treatment-related sequelae were also



similar. These authors emphasized that CRT for elderly patients was effective and safe, but they defined “elderly” as “ $\geq 65$  years” or “ $\geq 55$  years”, in accordance with the reports about RH. These age groups are usually not defined as “elderly.” Therefore, whether concurrent CRT is safe for elderly patients aged over 70 years or 75 years or older remains unclear.

However, to achieve further improvement in survival outcomes for elderly patients with cervical cancer, especially locally advanced disease, CRT is a necessary modality. After performing large and prospective studies, concurrent CRT for selected patients aged  $\geq 70$  or 75 years may provide excellent outcomes with acceptable toxicity. Published reports about elderly patients with cervical cancer are described in Table 2.

Authors (year)	No. of elderly patients (years)	Modality	Treatment results
Mitchell. (1998)	60 ( $\geq 70$ )	RT	OS rate: 46% (5-y) CSS rate: 58% (5-y)
Sakurai. (2000)	41 ( $\geq 80$ )	RT	OS rate: 33% (5-y) CSS rate: 65% (5-y)
Lindegaard. (2000)	114 ( $\geq 70$ )	RT	
Geisler. (2001)	62 ( $\geq 65$ )	Surgery	
Chen. (2003)	79 ( $\geq 70$ )	RT	
Brun. (2003)	31 ( $\geq 75$ )	Surgery, RT	OS rate: 42% (5-y)
Wright. (2005)	197 ( $\geq 70$ )	Surgery, RT, CRT	
Ikushima. (2007)	132 ( $\geq 75$ )	RT	OS rate: 49% (5-y) CSS rate: 66% (5-y)
Goodheart. (2008)	27 ( $\geq 65$ )	CRT	OS rate: 44% (5-y) CSS rate: 71% (5-y)
Magne. (2009)	113 ( $\geq 70$ )	Surgery, RT	OS rate: 89% (3-y)
Kunos. (2009)	103 ( $\geq 55$ )	CRT	OS rate: 56% (5-y)
Yoshida. (2010)	40 ( $\geq 75$ )	RT	OS rate: 58%, (3-y) CSS rate: 80% (3-y)
Kashima. (2010)	41 ( $\geq 60$ )	Surgery $\pm$ adjuvant RT	

RT: Radiotherapy, CRT: Concurrent chemoradiation, OS: Overall survival, CSS: Cause specific survival

Table 2. Published reports about elderly patients with cervical cancer

## 5. Conclusions

Selection of treatment modalities for elderly patients with cervical cancer is often limited compared to younger patients, but definitive RT, a combination of EBRT and ICBT is effective and safe. Indications for a surgical approach with or without adjuvant RT or concurrent CRT are still unclear because these aggressive modalities may cause severe treatment-related toxicity, especially for elderly patients. However, for locally advanced disease, CRT is an effective treatment. Therefore, large and prospective studies using CRT for patients aged at least  $\geq 70$  years with cervical cancer are needed. For RT, new techniques,

such as IMRT, IGBT or a combination of both, may help to reduce the RT-induced toxicity in both definitive and adjuvant treatment. In the near future, IMRT combined with IGBT with or without new chemotherapeutic regimens will be the standard cervical cancer treatment in aging women.

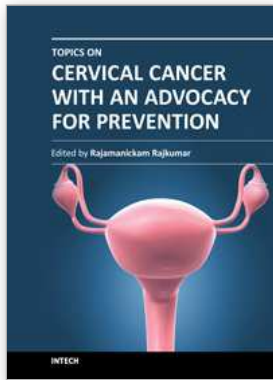
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## **Topics on Cervical Cancer With an Advocacy for Prevention**

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Cervical Cancer is one of the leading cancers among women, especially in developing countries. Prevention and control are the most important public health strategies. Empowerment of women, education, "earlier" screening by affordable technologies like visual inspection, and treatment of precancers by cryotherapy/ LEEP are the most promising interventions to reduce the burden of cervical cancer. Dr Rajamanickam Rajkumar had the privilege of establishing a rural population based cancer registry in South India in 1996, as well as planning and implementing a large scale screening program for cervical cancer in 2000. The program was able to show a reduction in the incidence rate of cervical cancer by 25%, and reduction in mortality rate by 35%. This was the greatest inspiration for him to work on cervical cancer prevention, and he edited this book to inspire others to initiate such programs in developing countries. InTech - Open Access Publisher plays a major role in this crusade against cancer, and the authors have contributed to it very well.

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