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Cervical Cancer with Radiotherapy Treatment

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A B S T R A C T

Cervical cancer is an abnormal growth of cells in the cervix, which its etiological agent is infected by the human papillomavirus. Globally, cervical cancer is the fourth most common cancer in women, one of the most frequently diagnosed cancer, and a cause of cancer-related death. The Global Cancer Statistics 2022, censused approximately 660,000 new cases and 350,000 deaths worldwide. Therefore, to contrast cervical cancer as a public health problem, the World Health Organization in 2020, conducted a global health strategy with tertiary interventions: (1) prevention through HPV vaccination; (2) screening and precancerous lesions treatment; and (3) adequate treatment of invasive cervical. Currently, there are three therapeutic modalities which are surgery, chemotherapy, and radiotherapy. These may include one or a combination of surgery, chemotherapy and radiotherapy. Radiotherapy is a major treatment in the management of cervical cancer, which uses high energy x-rays.

INTRODUCTION

Globally, cervical cancer is the fourth most common cancer in women and the most common gynecological cancer. Although the human papillomavirus (HPV) vaccination and screening are effective, cervical cancer is still a large global health issue, especially in low and middle-income countries due to a wide inequality in HPV vaccination coverage, access to preventive interventions, and socio-economic factors [1].

Cervical cancer is one of the most frequently diagnosed cancers and a cause of cancer-related death in women [2]. The last iteration of the Global Cancer (GLOBOCAN) Statistics 2022 censused approximately 660,000 new cases and 350,000 deaths worldwide in 2022. These both statistics are expected to escalate without broad interventions [3]. The total of

5-year overall survival rate for all stages is 67%, with the detail of 91% for early stage, 60% for locally advanced disease, and 19% for metastatic disease. Most of cervical cancer cases (~95%) are caused by persistent infection with high-risk HPV. The most common histologies are squamous cell carcinoma (~80%) and adenocarcinoma (~20%), whereas other histologic subtypes remain rare [1].

The single most important etiological agent of cervical cancer is infection by HPV. The connection between HPV and cervical cancer was established in the last 30 years based on the detection of HPV type 16 in cervical cancer tissue by Harald zur Hausen. HPV is approximated to infect around 291 million women in global. However, women under the age 25 have a significantly higher frequency [4].

To contrast cervical cancer as a public health problem, the World Health Organization (WHO) in 2020, conducted a global health strategy, being the first time ever that the world has committed to eliminate a cancer. Cervical cancer certainly is both preventable and treatable, and also able to reduce of burden, with tertiary interventions, ranging from primary prevention strategies to screening campaigns, until to effective treatment selections [2]. Generally, cervical cancer can be cure if it is diagnosed and treated at an early stage. Early-stage cervical cancer's (stages IA – IB2 and IIA1) treatment recommendation is surgery and proceed to do observation or adjuvant therapy (radiotherapy±concurrent chemotherapy) based on histopathologic risk factors on definitive pathology. Treatment for patients that is carefully selected, like conservative and fertility-sparing approaches may be taken into consideration. Standard of treatment for locally advanced cervical cancer (stages IB3 and IIA2 – IVA) is definitive concurrent chemoradiotherapy. However, recent research found out about the potential in improving this standard of treatment for the patients with locally advanced cervical cancer. Based on results of the KEYNOTE-A18 trial, the US Food and Drug Administration (FDA) recently approved adding pembrolizumab into concurrent chemoradiotherapy for patients with high-risk locally advanced cervical cancer. Furthermore, results from the INTERLACE trial presented at the 2023 European Society for Medical Oncology (ESMO) congress, demonstrated that induction chemotherapy before standard concurrent chemoradiotherapy provides a significant improvement in overall survival. Patients with metastatic (stage IVB), persistent, or recurrent cervical cancer should receive multidisciplinary treatment at tertiary referral centers. The management of these patients poses a major clinical challenge and relies on combined treatment modalities, including platinum-based chemotherapy±bevacizumab±pembrolizumab, locoregional treatments (surgery, radiotherapy), enrollment in clinical trials, and/or palliative care [1].

METHOD

A literature search identified a systematic review using studies related to mindfulness's physiological and psychological effects. The investigation was conducted through Pubmed, Science Direct, and Google Scholar databases using the keywords Cervical Cancer Treatment. The Inclusion and Exclusion Criteria are:

Inclusion criteria:

1. Full-text article
2. Original articles published in English
3. Publication date between 2019 – 2024
4. Respondents in the study were cervical cancer patients
5. Using the Randomized Controlled Trial research method

Exclusion criteria:

1. Narrative review
2. Article published not in English
3. Respondents in the study other than breast cancer patients
4. Using research methods other than Randomized Controlled Trial

RESULT AND DISCUSSION

Cervical Cancer

Cervical cancer is defined by the abnormal growth of cells in the cervix. Mostly at the area of the uterus that joins the vagina. It is a common type of cancer in women. Cervical cancer is prevalent in developing countries [5].

The most widely used for cervical cancer staging method is the International Federation of Gynaecology and Obstetrics (FIGO) guideline, which is divided into four stages: stage I, II, III, and IV. Stage I is when the cancer spreads beyond the inner lining of the cervix but is still confined to the cervix. Stage II is when the cancer has spread beyond the cervix but not the pelvic wall and lower third of the vagina. Stage III is when it reaches these region. Stage IV is described by cancer cells having metastasized to the bladder, rectum (stage IVA) and other parts of the body such as, the lungs, liver, and skeleton (stage IVB), by the hematogenous route [4].

Table 1. International Federation of Gynaecology and Obstetrics (FIGO) staging[4]

FIGO Stages	Definition
IA	Invasive carcinoma diagnosed only by microscopy, with max. depth of invasion <5 mm.
IA1	Stromal invasion <3 mm in depth
IA2	Stromal invasion ≥3 mm & <5 mm in depth.
IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than IA2.
IB1	Invasive carcinoma ≥5 mm depth of stromal invasion, and <2 cm in greatest dimension.
IB2	Invasive carcinoma ≥2 cm and <4 cm in greatest dimension.
IB3	Invasive carcinoma ≥4 cm in greatest dimension.
II	Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina.
IIA	Tumour without parametrial invasion or involvement of the lower one-third of the vagina.
IIA1	Clinically visible lesion <4 cm in greatest dimension with involvement of less than the upper two-thirds of the vagina.
IIA2	Clinically visible lesion >4 cm in greatest dimension with involvement of less than the upper two-thirds of the vagina.
IIB	Tumour with parametrial invasion but not up to the pelvic wall.
III	Tumour extends to pelvic wall and/or involves lower third of vagina, and/or causes hydronephrosis or nonfunctioning kidney, and/or involves pelvic and/or para-aortic lymph nodes
IB1	Invasive carcinoma ≥5 mm depth of stromal invasion, and <2 cm in greatest dimension.
IB2	Invasive carcinoma ≥2 cm and <4 cm in greatest dimension.
IB3	Invasive carcinoma ≥4 cm in greatest dimension.
II	Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina.
IIA	Tumour without parametrial invasion or involvement of the lower one-third of the

	vagina.
IIA1	Clinically visible lesion <4 cm in greatest dimension with involvement of less than the upper two-thirds of the vagina.
IIA2	Clinically visible lesion >4 cm in greatest dimension with involvement of less than the upper two-thirds of the vagina.
IIB	Tumour with parametrial invasion but not up to the pelvic wall.
III	Tumour extends to pelvic wall and/or involves lower third of vagina, and/or causes hydronephrosis or nonfunctioning kidney, and/or involves pelvic and/or para-aortic lymph nodes
IIIA	Tumour involves lower third of vagina, no extension to pelvic wall.
IIIB	Tumour extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney.
IIIC	Tumour involves pelvic and/or para-aortic lymph nodes, irrespective of tumour size and extent.
IV	Tumour invades mucosa of bladder or rectum (biopsy proven), and/or extends beyond true pelvis
IVA	Tumour has spread to adjacent pelvic organs.
IVB	Tumour has spread to distant organs.

Bagian pembahasan memaparkan hasil pengolahan data, menginterpretasikan penemuan secara logis, mengaitkan dengan sumber rujukan yang relevan. [Times New Roman, 12, normal], spasi 1. Format gambar png/jpg .

History of Cervical Cancer

The Greek physician Pericles Hippocrates was the first one to identify a new type of cancer whisch is cervical cancer that was found in 400 B.C.. At first, it was considered impossible to cure, but until some 2000 years later, the idea of the pathogenic mechanism was revealed from pioneer study by an Italian surgeon. In the middle of 19th century, Dr. Rigoni Stern noticed that it is rare among nuns to had a incidence of cervical cancer. All these result of studies has indications that the cause of cervical cancer is related to with sexual intercourse. Therefore cervical cancer was described as a highly transmissible diseases. In the year of 1976, a German Scientist named Zur reported later in his publication that a transmitting agents were discovered, called HPV DNA which is found in cervical cancer and warts. In 1985 Zur Hausen and Gissmann, together with their co-workers, identified the structure and sequence of HPV. Further later, discovery of HPV vaccine led to the milestone in curing the disease [5].

Epidemiology

Cervical cancer is the fourth leading cause of cancer incidence and mortality in women worldwide, with more than 85% of cases occur in low-resource countries. In 2022, there were a total of 662 301 new cases and 348 874 deaths globally. The cumulative lifetime risk of developing and dying from cervical cancer are 1.50% and 0.79%. There is an unequality burden of cervical cancer incidence in worldwide, due to a distinct socioeconomic gradient. Cervical cancer incidence and mortality rates are three and six times higher in low human development index (HDI) countries, than in high HDI countries. Regions with particularly high incidence and mortality rates are East and Southeast Asia (60% of global cases, 57.3% of deaths), sub-Saharan Africa (19% of cases, 23.1% of deaths), and

Latin America (9.5% of cases, 9.6% of deaths) [1], [3]. Patients in low HDI countries are more likely to be diagnosed at a later stage. Worldwide, around 40–50% of cervical cancers are diagnosed at an early stage, 35–40% at locally advanced stage, and 10–25% at metastatic stage. Geographic and socioeconomic diatinction in the incidence and global burden of cervical cancer indicate that there are inequalities in the availability of the HPV vaccine and accessibility to adequate screening and treatment of precancerous lesions [1].

Risk Factor

The main risk factor for cervical cancer is persistent HPV infection, such as HPV 16 and 18 which are the most common high-risk genotypes. More than 70% of cervical cancer diagnoses are infected by HPV 16/18 genotypes. In addition, other common risk factors like smoking, high number of sexual partners, and HIV infection, highlighting the importance of risk reduction strategies aimed at smoking cessation and HIV prevention [1].

HPV

Almost all cervical cancer cases are cause by the infection of human papillomavirus (HPV). HPV types are classified into two risk strains depending on their oncogenic potential. (1) Low-risk strains of HPV may be asymptomatic or cause anogenital warts, while high-risk strains are oncogenic. High-risk HPV is a sexually transmitted virus capable of establishing persistent infections that can resukt in precancerous lesions and cervical cancer. More than 99% of precancerous lesions (cervical dysplasia) and cervical carcinomas are caused by high-risk HPV infection [1], [6].

HPV is a non-enveloped, double-stranded DNA virus of 8 kilobase pairs. It contains a total of eight open reading frames, including two structural genes (*L1*, *L2*) as well as six early genes involved in viral replication (*E1*, *E2*, *E4*, *E5*, *E6*, *E7*). After HPV infection, distinct mRNA splicing patterns and multiple promoters control the expression of viral genes, allowing expression of gene products at different stages of the viral life cycle.[1]

Throughout the viral life cycle, *E6* and *E7* have an important function in increasing viral fitness and virion production. The E6 protein can directly interact with tumor suppressor protein (p53) and induce ubiquitin-dependent proteolysis. The E7 protein attach with pRb suppressor protein in order to ease the release of transcription factors such as E2F and induce gene transcription. This lead to a result in disruption of cell cycle regulatory pathways, resistance to apoptosis, and also dysregulated cell proliferation. Persistent HPV infection leads to integration of the viral genome into the cellular genome, promoting sustained expression of *E6* and *E7*, and loss of the *E2* gene, a repressor of the expression of these oncoproteins. Furhtermore, HPV integration induces genetic alterations, amplification of oncogenes, chromosomal rearrangements, and instability [1].

Majority of cervical cancer cases demonstrate integrated HPV genomes. In cases where the genome is in an episomal form, dysregulation
occurs by epigenetic modifications such as DNA methylation, histone modifications, non-coding RNA regulation and chromatin regulation [1].

Prevention and Screening

In 2020, WHO introduced a global strategy to erase cervical cancer as a public health issue, with the aim of achieving a global incidence of less than 4 per 100 000 women annually. The three main pillars of the strategy are: (1) prevention through HPV

vaccination; (2) screening and precancerous lesions treatment; and (3) adequate treatment of invasive cervical cancer. By 2030, this three main targets are expected to achieve in lowering the median cervical cancer incidence by 10%: (1) 90% of girls fully receive HPV vaccinations by the age of 15; (2) 70% of women underwent screening with high-performance tests for HPV detection by the age of 35 and later by the age of 45; (3) 90% of women receive adequate precancerous lesions treatment [1].

Prophylactic HPV vaccination has been proved to reduce the burden of HPV-associated disease. There are currently five commercial prophylactic HPV vaccines that are categorized as: two bivalent vaccines (HPV 16 and 18), two tetravalent vaccines (HPV 6, 11, 16, and 18), and one nonavalent vaccine (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58). Furthermore, there is emerging evidence on the safety and immunogenicity of a new nonavalent vaccine produced in Escherichia coli, a cost-effective and simple system for the production of L1 virus-like particles, which has the potential to reduce supply constraints and affordability of HPV vaccine [1].

Strategic treatment for cervical cancer prevention is primary screening, which include cervical cytology (Pap smear), HPV co-testing, and colposcopy (with biopsy). The main function of screening is to detect precancerous lesions in order to provide immediate treatment and relevant follow-up before the cancer develops [1].

The usability of polymerase chain reaction (PCR)-based tests for HPV genome detection have confirmed to be cost-effective while increasing sensitivity for detecting high-grade lesions. Several countries have implemented primary cervical cancer screening with HPV testing, along with triage testing to reduce the follow-up of transient infections. Unfortunately, there are numerous challenges to universal adoption of HPV-based screening, which has made primary screening coverage challenging, particularly in low-income and middle-income countries. The use of HPV testing in screening may improve the identification of adenocarcinoma. In resource-limited countries, screening still relies on direct visual inspection using acetic acid [1].

Treatment of Cervical Cancer

The choice of cervical cancer treatment determined by various criteria, including disease stage, histopathological type of tumor, regional and distant metastases, degree of tumor differentiation (grade-G), primary lesion size, way of primary tumor development, age and general condition of the patient. Currently, there are three therapeutic modalities which are surgery, hormone chemotherapy, and radiotherapy. These may include one or a combination of surgery, radiation and chemotherapy. Surgery as standalone and only therapeutic approach is used in preinvasive and early stage of invasive cervical cancer. For Ib and IIa stages, surgery and radiation are combined and also only radiation is used in IIb, IIIa, IIIb and IVa. In stage IVb, are used chemotherapy and locoregional radiotherapy[4], [7].

1. **Surgery**

   Surgery is a popular and effective method of treating various microinvasive stage of cancers since it affect the physical removal of cancerous tissue. It can also be used to eliminate metastatic tissue. Currently, there are a number of surgery types to treat cervical cancer, such as total hysterectomy, radical hysterectomy, loop electrosurgical excision procedure (LEEP), conization, trachelectomy, and also cryosurgery. The type of surgical treatment is depend on the disease stage

and extent of spread. As example, total hysterectomy with or without salpingo-oophorectomy (a surgical procedure to remove one or both ovaries), is the choice for women who have finished childbearing. Radical hysterectomy is most commonly used for bigger cervical cancer lesions (up to 4 cm in size) and require complete resection of the uterus, cervix, parametria, and cuff of the upper vagina. The Laparoscopic Approach to Cervical Cancer (LACC) study found that radical hysterectomy performed using laparoscopy was associated with an increased risk of recurrence, loss of fertility and probable urinary dysfunction in the long-term. Women at reproductive age with early stage disease require more conservative treatment approach and fertility-sparing surgeries, such as LEEP, conization and trachelectomy. LEEP remove abnormal tissue from the cervix using a thin, fine wire and can be performed under local anaesthesia in low-cost healthcare facilities, as in LMICs [4].

Surgery for cervical cancer, however, have advantages and disadvantages. This treatment have clinically proven to be highly effective, an one-time procedure and also can be given in combination with other treatments. But, it may require a hospital stay of up to 1 week and need a long recovery time [8].

2. Chemotherapy

Chemotherapy is an essential part of the standard cervical cancer treatment regimen and is generally administered as an adjuvant therapy following surgery when poor prognostic tumour features increase the risk of recurrent disease, in combination with radiotherapy. For the past 30 years, the most effective single agent to cure cervical cancer is the platinum-based chemotherapeutic, cisplatin. However, despite initial patient response to cisplatin, increased resistance during the treatment is often reported and this reduces the efficacy of additional second-line platinum-based chemotherapeutics. Studies have found that combining cisplatin with other agents is potentially more effective than single drug treatment [4].

Chemotherapy is mostly used for locally advanced cervical cancer and also often combined with radiotherapy (chemoradiotherapy). Although the goal of this regimen is to reduce the recurrence of the disease, it may cause side effects and chronic morbidity. It improves overall and progression-free survival and reduces the incidence of both local and distant cervical cancer recurrences. Palliative chemotherapy can improve quality of life and relieve disease symptoms, though it may not effectively reduce tumour size [4].

Chemotherapy for cervical cancer have the advantages and disadvantages. This treatment have clinically proven to be highly effective and as previously mentioned it can be given in combination with other treatment. However, the treatment course can be long (3–4 treatment week cycles, which are repeated at least 6 times), cause some side effects, like hair loss, and an increased risk of acquiring infections [8].

3. Radiotherapy

Radiotherapy is a major treatment in the management of cervical cancer, which uses high energy x-rays. There are three types of radiation therapy that currently used for cervical cancer treatment which are external beam radiation therapy (EBRT), intensity-modulated radiotherapy (IMRT), and brachytherapy with intracavitary

radiotherapy (ICR). Superior diagnostic tools like magnetic resonance imaging (MRI) and computerized tomography (CT) scans have supported to improve the evaluation of the primary tumor, extent of tumor invasion and metastasis which then improved radiotherapy planning. In summary, EBRT is the most common form of radiotherapy, which aims high energy radiation beams from outside the body into the tumor and. IMRT is more advanced form of radiotherapy, that involves the manipulation of photon and proton radiation beams to correspond to the tumor's shape. It is used for both cancerous and non-cancerous tumors. Brachytherapy spares nearby tissues by either delivering a high dose of radiation to the tumor or a radioactive implant is inserted at the site of the tumor [4].

Radiotherapy for cervical cancer have clinically proven to be highly effective and can receive treatment on an outpatient basis. Although 68.3% of patients with stage IIA-IIIB cervical cancer experience a complete treatment, radiotherapy itself is unable to stop the growth of locally advanced disease in 20–50% of women. Radiotherapy can be given in combination with other treatments. Therefore, to increase the efficiency of radiotherapy, it is often used in conjunction with chemotherapy, especially for larger cervical cancer lesions (greater than 4 cm in width) [4], [8].

Radiotherapy

Radiotherapy for cervical cancer generally is a combination of EBRT and brachytherapy with intracavitary radiotherapy (ICR), in order to balance EBRT and ICR so that it increases the possibility of loco-regional tumor control and at the same time it can reduce the risk of treatment [9].

The total dose of radiotherapy that can be performed to the pelvis by EBRT is restricted by the resistance of normal pelvis tissues, including urinary bladder as well as small and large bowels. Hence, ICR is needed to deliver cancerocidal doses to the gross tumor in the cervix and parametrium [9].

Combining Radiotherapy with chemotherapy may increase the chances to cure patients with advanced locoregional disease. The main purpose of EBRT is to eliminate regional disease and to shrink the central tumor, to facilitate subsequent ICR. Ideally, the entire treatment should ended not more than 8 weeks; to ensure effective disease control [9].

Advancements in image-based technical, like three-dimensional conformal radiotherapy, intensity-modulated radiotherapy, and image-guided radiotherapy, enable more accurate radiation delivery. This can lead to dose escalation, improving tumour control, and reduced toxicity by minimizing the dose around normal tissues. However, these method need advanced technology and educated personnel, making them unachievable in low-income countries with underdeveloped health systems [9].

1. **Radiotherapy Equipment**
   a. **External Beam Radiation Therapy (EBRT)**

      EBRT use a teletherapy machine such as linear accelerator (linac) or telecobalt machine, where radiation is delivered as a beam from a radioactive source. Modern teletherapy machines are isocentrically positioned, so that the beam can rotate around the patient at a fixed source-to-axis distance 100 cm (linacs) or 80 cm (telecobalt machines). Linacs use electricity to generate high-energy

X-rays (15– 25 MeV), allowing equal radiation distribution at the deep tissues with relative sparing of superficial tissues, while telecobalt machines release gamma rays from a radioactive cobalt (cobalt-60) source kept in the head of the machine [9].

Telecobalt machines have been a leading provider of EBRT since the 1950s. However, in many high and middle-income countries, linacs have largely replaced telecobalt machines as the most common radiation source in radiotherapy [9].

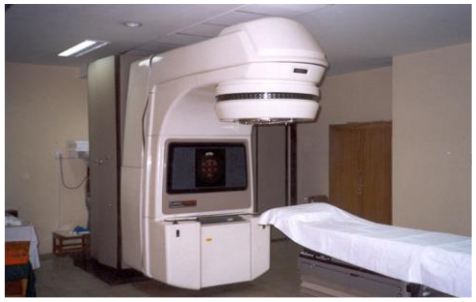

Figure 1. Linear accelerator (linac)[9]

Over five generations, linacs have evolved into compact, versatile, efficient, and affordable, with a diverse energy sources. Linacs need more advanced maintenance in terms of medical physics and dosimetry support. It require continuous electricity and consume large amounts of electricity. In contrast, telecobalt machines (cobalt-60) is replaced after two or three half-lives. Low-income developing countries prefer telecobalt machine due to its affordable cost and reliable performance. Finally, manual treatment planning has been replaced by computerized treatment planning systems in many countries [9].

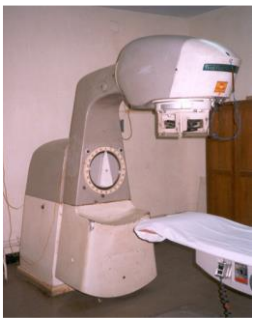

Figure 2. Telecobalt machine[9]

b. Intracavitary Radiotherapy (ICR)

In ICR, radioactive sources are inserted into the uterine cavity and vagina to release a very radiation dose to the cervix and uterus with relative sparing of surrounding tissues, like the bladder, rectum, small bowel, and superficial soft tissues. Before, ICR methods required the placement of sealed radioactive sources, for example, radium-226 or caesium-137. Unfortunately, it is not optimal from a radiation protection perspective. Nowadays, automatic afterloading devices using empty applicators are use [9].

Radiation source is being placed in a non-radioactive metallic capsule. After accurate positioning of the delivery applicators in the uterine cavity and vagina using X-ray, ultrasound, or CT imaging, the radiation sources are afterloaded. After the radiation dose is delivered, the sources are removed manually by a radiation oncologist. Other option that can be done is using a computeraided remote afterloading machine, which automatically removes the sources

once the treatment is done. Precise applicator placement is important for improved local control and reduced morbidity [9].

A computer is used in treatment planning to calculate the amount of time needed to deliver the prescribed dose of radiation to the tumor. Although low-dose-rate brachytherapy with caesium-137 was used before, high-dose-rate brachytherapy with iridium-192 currently become more popular. High-dose-rate brachytherapy reduce radiation exposure to medical personnel and allows a shorter treatment time and greater patient convenience. In terms of locoregional control and complication rates, high-dose-rate brachytherapy performs similarly to low-dose-rate brachytherapy [9].

2. Radiotherapy Dose

It is important to prescribe the suitable dose for radical and palliative radiotherapy so that the dose is measure correctly to prevent unwanted damage to normal tissues. Radical treatment refers to prescription of a high dose of radiation with curative intent, whereas palliative treatment refers to prescription of lesser doses of radiation (which by itself does not cause any toxicity or complications) [9].

The choice of radiotherapy dose and delivery techniques are based on normal tissue tolerance and the cancerocidal dose required to destroy the cancer cells in radical treatments. The normal tissue tolerance dose varies and depends on the proportion of tissues treated [9].

Radiotherapy dose is described as grays (Gy) or centigrays (cGy = 0.01 Gy). The total radiation dose is usually divided into small fractions of radiation (180/200 cGy per fraction), which gradually adding up to the total dose over time. Radiation is usually delivered as one fraction each day, 5 days per week for 4–8 weeks. But it is even better over 4–8 weeks, which leads to maximum cancer cell kill while maximal recovery of and minimal damage to normal cells. During the interval between the fractions, normal cells recover much faster than tumour cells [9].

Radical radiotherapy doses are typically 35–40 Gy in 15–20 fractions over 3–4 weeks for highly radiosensitive lymphomas and germ-cell tumors. For most squamous cell carcinomas, the doses range from 50 Gy in 15 fractions over 3 weeks to 65–70 Gy in 30–35 fractions over 6–7 weeks. Palliative radiotherapy doses are on the order of 30 Gy in 10 fractions over 2 weeks or 20 Gy in 5 fractions over 1 week, or even a single dose of 8–10 Gy [9].

The skin may be marked to indicate the radiotherapy portal where treatment should be delivered. The patient should be immobilized so that the target region receives the intended dose. The daily treatment setup is reproduced by in-room laser alignment to either skin marks or fixation aids such as thermoplastic devices [9].

3. Survival outcomes after radiotherapy

The 5-year survival rates after radiotherapy for cervical cancer are as follows: stage IA, 95%; stage IB1, 85%; stages IB2 and IIA, 60–65%; stage IIB, 50%; stage III, 30–40%; stage IVA, 10–15%; and stage IVB, 5% [9].

4. Consequences of radiotherapy for cervical cancer

Radiotherapy may cause acute side effects such as abdominal cramps, rectal discomfort, diarrhoea, pelvic pain, skin toxicity, lymphedema, sexual

dysfunction, occasional rectal bleeding, dysuria, increased urinary frequency, nocturia, haematuria, erythema, dry/moist desquamation of the perineum or intergluteal fold, radiation vaginitis, and superficial ulceration of the vagina. Late effects include proctitis/ cystitis (3–10%), vaginal stenosis, vaginal atrophy, dyspareunia, anal incontinence, vesicovaginal or rectovaginal fistula, lumbosacral neuropathy, and femoral neck fracture. Most of them can be a risk of long term side effect [9].

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