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Cervical cancer treatment and nursing considerations: Best practices for effective care

by Jodi Hyman, Christa Slatnik, and Michelle Ellwood

ABSTRACT

Over the past several decades, there has been excellent progress in cervical cancer prevention and early detection. However, there are still many Canadian woman who will be diagnosed with cervical cancer and will require active treatment. Advancements in personalizing treatment options based on specific staging and fertility-sparing preferences have helped decrease morbidities for some while ensuring well-needed aggressive treatment for others. Surgical procedures, for example, offer a variety of options with curative intent, particularly for those with earlier stage disease. Once the cancer has spread beyond the cervix to locally advanced stages 2 and 3, the combination of chemotherapy and radiation tends to be the mainstay treatment option. Finally, as cancer becomes more advanced into later stages 3 and 4 disease, utilizing traditional chemotherapy with the addition of novel drugs, such as monoclonal antibodies and immune check point inhibitors, offers hope where it was once lacking. This article focuses on these varying treatment options and identifies how nurses are in the prime position to help patients improve overall understanding, tolerance, and continuity of their treatment plan.

INTRODUCTION

Prevention, diagnosis, and treatment of cervical cancer has evolved drastically over the past 30 years. The scientific community has identified human papillomavirus (HPV) as a causal agent in the development of cervical cancer (Caird et al., 2022). This discovery subsequently led to the development and implementation of an HPV vaccination, as well as advancements in testing technologies and their application in diagnosing and screening for high-risk HPV. Taken together, these steps are critical, as Canada transitions to eliminate cervical cancer. As a result of the World Health Organization's global call for cervical cancer elimination initiative, Canada has committed to achieving cervical cancer elimination by 2040 (Canadian Partnership Against Cancer, 2021). However, until Canada can actualize this goal, there are woman with cervical cancer who require treatment to cure or control their disease.

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The aim of this article is to provide an overview of the current Canadian treatment options for women with a diagnosis of cervical cancer, discussed in accordance with cervical cancer stage. By understanding each disease stage and corresponding treatments, nurses have the ability to provide evidence-informed care and education to their patients, ultimately improving the overall cancer-patient journey.

CERVICAL CANCER STAGING

In 2018, the International Federation of Gynecology and Obstetrics (FIGO) staging classification system for cervical cancer was updated to include clinical staging and radiological imaging in the staging of the disease (see Table 1). This led to improvements in the clinician's ability to obtain information regarding possible lymph node involvement and, thereby, more accurately guide treatment decisions and prognostic outcomes (Salib et al., 2020). Disease staging and positive nodal involvement are critical prognostic factors for patients, as these factors influence the five-year survival rate (Salib et al., 2020).

Magnetic resonance imaging (MRI) is used to measure tumour size, to assess for parametrial involvement, and to gauge vaginal involvement. In patients diagnosed with early stage 1 disease, the microinvasive disease may not be observable with MRI. However, pre-operative MRI will aid in visualizing the cancer, rule out skip lesions (multifocal lesions that can be patchy, skipping areas that are normal), and assess the lymph nodes. Nodal disease is typically assessed with positron emission tomography (PET) or computed tomography (CT) scans.

STAGE I-IB2 – SURGICAL PROCEDURES

Surgery tends to be the mainstay of treatment options for early-stage disease. In a recent meta-analysis Wang et al. (2021) concluded surgery and radiation are equally effective in the treatment of early-stage disease. Surgery is generally favoured over pelvic radiotherapy, due to the increased morbidity associated with pelvic radiation (Matsuo et al., 2019). Side effects, such as ovarian failure, vaginal stenosis, and bowel dysfunction are associated with pelvic radiotherapy and can impact a survivor's quality of life significantly. As such, pelvic radiation is reserved for treatment of disease that is not surgically resectable or for patients that are deemed not to be surgical candidates (Landoni et al., 1997).

Table 2, FIGO Staging and Surgical Options, summarizes the diverse cervical cancer options used to treat Stage 1 to 1B2 cervical cancers, along with recommendations based on recent research, pathological findings, cancer stage, and patient fertility preference. Stage II disease does not receive surgical resection, due to the parametrial involvement that defines Stage II disease (Altman et al., 2019). Surgical interventions

Table 1

Modified FIGO Staging Table

Stage	FIGO Definition
I	Confined to cervix
IA	≤ 5 mm depth
IA1	≤ 3 mm depth
IA2	≤ 3 mm and ≤ 5 mm depth
IB	≥ 5 mm depth
IB1	≤ 2 cm maximum diameter
IB2	> 2 cm and ≤ 4 cm maximum diameter
II	Beyond the uterus but not involving the lower one-third of the vagina or pelvic sidewall
IIA	Upper two-thirds of vagina
IIB	Parametrial invasion
III	Lower vagina, pelvic sidewall, ureters, and lymph nodes
IIIA	Lower one third of vagina
IIIB	Pelvic sidewall
IIIC	Pelvic and para-aortic lymph node involvement
IV	Adjacent and distant organs
IVA	Rectal and bladder involvement
IVB	Distant organs outside pelvis

Note. Table 1 adapted from 2018 FIGO Staging Classification for Cervical Cancer: Added Benefits of Imaging (Salib et al., 2020).

include conization (removal of cone-shaped portion of the cervix) with cone biopsy or electrosurgical excision procedure (LEEP), radical trachelectomy (fertility sparing surgery), simple hysterectomy, or radical hysterectomy. For the procedure to be considered suitable treatment, the resulting final surgical pathology must show negative surgical margins. The management of positive margin(s) varies from repeat conization to adjuvant post-operative radiotherapy (National Comprehensive Cancer Network [NCCN], 2023).

The ConCerv trial, led by Schmeler et al. (2021) impacted current surgical options for women with early stage, low-risk cervical cancers. This prospective trial reviewed cervical cancer data from stage 1A2–1B1. It aimed to identify if patients with squamous cell or grade 1–2 adenocarcinoma had differing rates of reoccurrence after undergoing a cone versus a simple hysterectomy. Trial criteria specified no lymph-vascular space invasion (LVSI), negative margins on cone, tumours with less than 2 cm, and less than 10 mm depth of invasion. (Schmeler et al., 2021). ConCerv found that there was no difference in the three-year survival rates (3.5%) for patients who underwent a conization versus a simple hysterectomy. ConCerv results are reflected in the surgical recommendations made in Table 2.

Table 2

Surgical Guidelines Based on FIGO Staging

2018 FIGO Staging	Surgical options
Stage 1A1: 0–3 mm depth of invasion	Conization (Cone biopsy, cold knife, LEEP), +/- sentinel SLN +/- lymph node dissection LND
	Simple or radical trachelectomy, based on individual patient characteristics and centre, +/- SLN, +/- LND
	Simple hysterectomy, +/- SLN, +/- LND
Stage 1A2: 3 mm–5 mm depth of invasion	Conization with pelvic lymph node (PLN) if ConCerv trial (Schmeler et al., 2021) criteria met. SLN or LND
	Simple or radical trachelectomy based on individual patient characteristics and centre, if ConCerv trial criteria met. SLN or LND.
	Simple hysterectomy for those who meet Shape trial criteria. SLN or LND
	Radical Hysterectomy for those who do not meet SHAPE Criteria.
Stage 1B1: maximum depth of 5 mm and less than 2 cm diameter	Conization with LN if meets ConCerv trial criteria. SLN or LND
	Simple or radical trachelectomy with LN if meets ConCerv trial criteria. SLN or LND
	Simple hysterectomy for those who meet SHAPE trial criteria. SLN or LND
	Radical Hysterectomy for those who do not meet SHAPE trial criteria. SLN or LND.
Stage 1B2: maximum depth of 5 mm and 2–4 cm in diameter	Radical trachelectomy with select patients.
	Radical hysterectomy with SLN or LND and possible para-aortic nodes

Note: 1A1 disease with lymph-vascular space invasion (LVSI) and all other stages of disease require sentinel lymph nodes (SLN) mapping or full lymph node dissection (LND), dependent on centre practices (NCCN 2023).(Plante et al., 2024; Schmeler et al., 2021)

Radical hysterectomy was once the standard treatment for cervical cancer. However, it is associated with possible long-term side effects that can significantly impact a survivor's quality of life. Women who undergo a simple hysterectomy have their uterus and the cervix removed. A radical hysterectomy is more extensive and involves removing the uterus, cervix, part of the vagina, and the parametrium.

The SHAPE trial was conducted to evaluate further the surgical alternative of simple hysterectomy as a less invasive surgical option. This prospective study reviewed cervical cancer data from stage 1A2–1B1, with any grade of histology, to identify if there were differing rates of recurrence after a simple hysterectomy versus a radical hysterectomy. Trial criteria also included positive or negative margins, tumours less than 2 cm, and positive LVSI. SHAPE showed that three years after surgery, the rate of reoccurrence was 3.5%, regardless of the type of hysterectomy (Plante et al., 2024). SHAPE trial findings are reflected in Table 2.

Surgical considerations

Early-stage disease has a lower risk of cancer reoccurrence and viable fertility-sparing surgical options, as shown in the ConCerv trial. Fertility sparing options include conization and simple or radical trachelectomies (surgery to remove the cervix, the upper part of the vagina, and surrounding supporting tissues). Desire to preserve fertility must be explored with patients and include discussions incorporating statistics on survival rates, reoccurrence rates, as well as future pregnancy recommendations (Benedict et al., 2016). A recent position statement on fertility preservation is an excellent guide for nurses in their dialogue with patients (CANO et al., 2024).

When a patient is pre-menopausal at the time of a simple or radical hysterectomy, consideration ought to be given to the conservation of the ovaries. However, there is no current treatment standard in Canada at this time. Treatment-induced menopause impacts quality of life for cancer survivors. As such, the risks associated with premature ovarian failure, as well as the importance of hormone replacement therapy should be discussed, if surgically induced menopause is a risk (Singh et al., 2010).

The risk of metastatic disease to the ovaries varies, based on the cervical cancer sub-type. However, the risk is low in early-stage disease. Squamous cell carcinoma brings a risk of 1%–3% risk of metastatic disease to the ovaries, with the ovaries commonly preserved at the time of surgery. Adenocarcinoma has a higher risk at 3%–10% (Shimada et al., 2006), so intraoperative examination and decision-making about the procedure is key. If there are no abnormalities noted during an intraoperative examination, the ovaries of a pre-menopausal person are left *in situ,* and a bilateral salpingectomy is performed to preserve the ovarian function. When disease is highly suspected, or a patient is post-menopausal, a bilateral salpingo-oophorectomy is performed.

An open surgical approach is always used should a radical hysterectomy be required. The Laparoscopic Approach to Cervical Cancer (LACC) Trial showed that cervical cancer survivors who underwent minimally invasive surgery had lower rates of disease-free survival and decreased overall survival when compared to survivors who underwent an open procedure at the time of a radical hysterectomy (Ramirez et al., 2018). 1A1 disease treated with a simple hysterectomy can be performed using a laparoscopic approach. However, in 1A2 to 1B1 disease, tumour factors must be reflected when considering laparoscopic versus laparotomy. Expert opinion recommends avoiding use of uterine manipulators when performing laparoscopic surgery with 1A2 to 1B1 disease, but studies regarding use of uterine manipulators are ongoing. Overall, there are a variety of surgical techniques to consider in early-stage disease, guided by the extent of the disease and the individual's desire to preserve fertility.

Nursing considerations

Nurses play a vital role in ensuring a smooth surgical experience from pre-op planning to post-op recovery. Enhanced Recovery After Surgery (ERAS) is an evidence-based care pathway aimed to help reduce surgical complications, enhance patient recovery, and reduce hospital stay (Altman et al., 2019). The ERAS protocol includes pre-operative methods such as patient education and counselling, prehabilitation, smoking and alcohol cessation, and carbohydrate loading, while post-operative components include early mobilization, early feeding, and early drain/catheter removal. Although compliance with the ERAS protocol can be challenging, due to the increased risk of bladder dysfunction after a radical hysterectomy, early removal of the catheter should be attempted due to known benefits of ERAS in this patient population (Nelson et al., 2023).

Education based on best practice should begin in the pre-operative period and reflect the ERAS guidelines. This includes information regarding preparation for surgery, the surgical procedure, and the risks; further, what to expect during the post-operative course; and when to seek medical attention ought to be shared with the patient (Altman et al., 2019).

A recent study found that nurses' ability to meet the humanistic care-demands of cancer patients directly affected the level of psychological distress experienced in the post-op course (Ma et al., 2024). This was especially the case in post-op gynecological patients with individualized care plans; nurses were able to alleviate the level of psychological suffering women experienced post-operatively through meeting the individual needs of the person (Ma et al., 2024). Additionally, nurses can support relaxation techniques that can assist in managing various pre- and post-op patient symptoms such as anxiety, pain, and nausea. Relaxation techniques can include the use of interventions such as music, guided imagery, and muscle relaxation (Santana et al., 2023). Overall, with the combination of counselling patients about ERAS methods and encouraging relaxation techniques, nurses have the ability to improve the perioperative experience of patients undergoing surgery for early-stage cervical cancer.

STAGE II AND III – CHEMOTHERAPY WITH CONCOMITANT RADIATION

Among the variety of therapeutic approaches available when treating cervical cancer, the integration of cisplatin chemotherapy with radiation therapy has established itself as a critical component in the management of cervical cancer over the past 25 years (Gennigens et al., 2021; Rose et al., 1999; Pang et al., 2022). In cases of locally advanced cervical cancer, such as Stage II and III, the combination of weekly cisplatin chemotherapy and radiation therapy is typically considered the standard therapeutic approach (Chuang et al., 2016; Gennigens

et al., 2021; Herter et al., 2023; National Cancer Institute [NCI], 2024; Pang et al., 2022).

McCormack et al., (2024) recently published the results of the INTERLACE trail, which was a multicentre, randomized phase 3 trial conducted at 32 medical centres internationally. This trial concluded that there is an 8% overall survival benefit at the five-year mark in those who received carboplatin and paclitaxel for six cycles prior to current standard of care. This will likely become the new standard therapeutic approach to care for this group of patients.

Cisplatin, a cytotoxic platinum-based chemotherapy agent, causes DNA damage in cancer cells, thereby preventing their ability to proliferate and, in turn, triggering cell death. Simultaneously, radiation therapy uses high-energy X-rays/radiation to eradicate or stop the growth of cancer cells. When used together, cisplatin enhances the sensitivity of cancer cells to radiation, ultimately augmenting the therapeutic efficacy of radiation therapy (Herter et al., 2023). The typical chemoradiation regimen includes ~25–30 fractions/doses of external beam radiotherapy (EBRT) plus a median of 6 fractions of brachytherapy HDR, with five to six weekly doses of cisplatin intravenously (Wang et al., 2023). Treatment holidays are discouraged because of the negative impact on the rate of cure; all radiation should be completed within eight weeks (Pang et al., 2022).

Although one would suspect that removing the cancer tumour would provide a higher benefit, surgery alone is not likely to be curative. Surgery followed by radiation has shown higher rates of complications compared with primary chemoradiation (Pang et al., 2022). With that said, given the majority of cervical cancer diagnoses occurs in women living in middle- and low-income regions, access to daily radiation with weekly chemotherapy may be limited. Thus, surgical intervention may be required in some cases when chemoradiation is not accessible (Chuang et al., 2016).

The combination of cisplatin chemotherapy with radiation therapy offers a variety of advantages in the management of cervical cancer. For example, cisplatin's ability to sensitize cancer cells to radiation enhances tumour response causing superior tumour regression and disease control. Although combination therapy is typically preserved for locally advanced cervical cancers, it also allows the opportunity to offer organ preservation in early-stage cervical cancer and prevent the need for radical surgical interventions in some cases (Lin et al., 2020). There is also extensive clinical evidence supporting the superiority of combining cisplatin with radiation therapy, leading to enhanced overall survival rates and reduced risks of cancer recurrence compared to radiation therapy alone (Herter et al., 2023). Ultimately, the synergistic effect between cisplatin and radiation therapy results in an enhanced anti-cancer effect, exceeding the individual efficacy of each modality.

Adverse effects

Despite the benefits of combination therapy, it is not without challenges and potential adverse effects. Common side effects associated with cisplatin chemotherapy include nausea, vomiting, fatigue, renal and hematologic toxicity (Wang et al., 2023; see Table 3). If a patient has pre-existing chronic renal failure or significant baseline neuropathy, weekly low-dose carboplatin should be considered instead of cisplatin. However, if renal dysfunction is caused by malignant ureteral obstruction, a common side effect of cervical cancer, an attempt at normalizing renal function should be pursued with ureteral stenting or nephrostomy with hopes to increase eligibility of cisplatin (Pang et al., 2022).

Radiation therapy may induce skin irritation, vaginal dryness, radiation induced proctitis and cystitis, gastrointestinal disturbances, and fatigue (Wang et al., 2023). In addition, the synchronous use of cisplatin and radiation therapy may intensify these side effects, requiring attentive monitoring and comprehensive supportive care measures. Fortunately, radiation therapy has evolved over the past three decades with better techniques that allow for a more targeted approach, not only improving survival, but also creating less damage to surrounding healthy tissues (Gennigens et al., 2021; Wang et al., 2023).

Nursing considerations

Nurses are critical to ensuring optimal symptom management with hopes to help patients complete the duration of their treatment. Not only can nurses help prepare patients for what to expect before starting combination therapy, they can ensure patients are empowered to prevent some side effects whenever possible. For example, guiding patients on foods that can help decrease the severity of diarrhea can empower patients to know they have some control over the significance of the loose stool they may experience. If patients do develop some side effects, nurses can help with guiding self-care management between the patient's weekly check-in appointments.

As the use of cisplatin-based chemotherapy combined with radiation therapy in cervical cancer treatment has evolved, significant advancements in the combination are on the horizon. For example, targeted agents could disrupt specific molecular pathways that cause cancer progression and may have the ability to increase the efficacy of chemoradiation therapy while minimizing systemic toxicity (Lin et al., 2020). Immunotherapy also shows promise by utilizing the body's immune system to recognize and eliminate cancer cells when integrated with cisplatin and radiation therapy, possibly improving treatment response rates and prolonging survival (Herter et al., 2023; Lin et al., 2020). Finally, with the evolution of genomic profiling and precision medicine, it is anticipated that clinicians will be able to identify better patients who most likely would benefit from cisplatin-based chemotherapy and radiation therapy, in turn optimizing therapeutic outcomes while mitigating undue toxicity (Lin et al., 2020).

Ultimately, the recently published INTERLACE trial concluded that a short course of induction chemotherapy followed by the combination of cisplatin chemotherapy and radiation therapy represents an impressive therapeutic strategy in the fight against locally advanced cervical cancer (McCormack et al., 2024). While offering significant benefits in tumour control and overall survival, this combination therapy requires careful prevention, and attention to, or management of, potential side effects. Continuing research focused on advancing targeted therapies, immunotherapy, and precision medicine in conjunction with chemoradiation, shows potential to improve

Table 3

Acute and Late Toxicity of Intensity-Modulated Radiotherapy (IMRT) with Concurrent Chemotherapy (n = 98)

	Total (n = 98)		Tumor Size (mm) 40–<60 mm (n = 67)		≥60 mm (n = 31)		p-Value
	n	(%)	n	(%)	n	(%)	
Side effects							0.167
No	3	(3.06%)	1	(1.49%)	2	(6.45%)	
Yes	95	(96.93%)	66	(98.51%)	29	(93.55%)	
Nausea grade							0.152
Grade 1	17	(17.35%)	15	(22.39%)	2	(6.45%)	
Grade 2	24	(24.49%)	15	(22.39%)	9	(29.03%)	
Grade 3	1	(1.02%)	1	(1.49%)	0	(0.00%)	
Vomiting grade							0.803
Grade 1	10	(10.20%)	7	(10.45%)	3	(9.68%)	
Grade 2	12	(12.24%)	9	(13.43%)	3	(9.68%)	
Grade 3	1	(1.02%)	1	(1.49%)	0	(0.00%)	
Diarrhea grade (acute)							0.006 **
Grade 1	35	(35.71%)	26	(38.81%)	9	(29.03%)	
Grade 2	28	(28.57%)	23	(34.33%)	5	(16.13%)	
Grade 3	8	(8.16%)	2	(2.99%)	6	(19.35%)	
Hemoglobin grade							0.117
Grade 1	16	(16.33%)	12	(17.91%)	4	(12.90%)	
Grade 2	45	(45.92%)	32	(47.76%)	13	(41.94%)	
Grade 3	12	(12.24%)	5	(7.46%)	7	(22.58%)	
Leukopenia grade							0.139
Grade 1	17	(17.35%)	13	(19.40%)	4	(12.90%)	
Grade 2	22	(22.45%)	12	(17.91%)	10	(32.26%)	
Grade 3	40	(40.82%)	31	(46.27%)	9	(29.03%)	
Thrombocytopenia grade							0.142
Grade 1	48	(48.98%)	39	(58.21%)	9	(29.03%)	
Grade 2	5	(5.10%)	2	(2.99%)	3	(9.68%)	
Grade 3	2	(2.04%)	2	(2.99%)	0	(0.00%)	
Grade 4	1	(1.02%)	1	(1.49%)	0	(0.00%)	
Radiation proctitis grade (long term)							0.386
Grade 1	14	(14.29%)	10	(16.39%)	4	(12.90%)	
Grade 2	9	(9.18%)	5	(7.46%)	4	(12.90%)	
Grade 3	11	(11.22%)	8	(11.94%)	3	(9.68%)	
Radiation cystitis grade (long term)							0.624
Grade 1	8	(8.16%)	6	(8.96%)	2	(6.45%)	
Grade 2	7	(7.14%)	4	(5.97%)	3	(9.68%)	
Grade 3	13	(13.27%)	10	(14.93%)	3	(9.68%)	
Rectovaginal fistula [a]							1.000
No	92	(93.88%)	63	(94.03%)	29	(93.55%)	
Yes	6	(6.12%)	4	(5.97%)	2	(6.45%)	

Chi-Square test. [a] Fisher's Exact test. ** $p < 0.01$.

Note. Chi-square test; 1Fisher's Exact test; **p < 0.01.
(Wang et al., 2023)

treatment outcomes and enhance the quality of life for individuals dealing with cervical cancer.

STAGE IV – SYSTEMIC THERAPY FOR METASTATIC CERVICAL CANCER

Until recently, there were few advances in systemic treatment for cervical cancer patients with metastatic disease. For several years, the mainstay of treatment was platinum chemotherapy plus or minus targeted therapy with bevacizumab (Gopu et al., 2021). Systemic cancer therapy is now becoming more complex everyday with the advancements in genomics and discoveries of new drug pathways to kill cancer cells.

The long-standing use of a 21-day regimen with cisplatin or carboplatin and paclitaxel is a familiar regimen in the gynecologic oncology world. It has been well tolerated by patients over the years with the addition of preventative antiemetic routines. The addition of bevacizumab has further improved overall survival, but it is associated with adverse effects (Tewari et al., 2014). Bevacizumab is a monoclonal antibody that inhibits vascular endothelial growth factor (VEGF) which is a key factor in angiogenesis. The most common side effects for bevacizumab include bleeding, fatigue, hypertension, proteinuria, headache, diarrhea, venous thromboembolism, nausea, and vomiting. Patients are asked to monitor their blood pressure in case antihypertensive therapy is required (Drug Formulary, 2023). Proteinuria is also monitored using urinalysis prior to each dose administered. Bevacizumab may also impair wound healing and should not be administered within 28 days of surgery, or until the wound is healed (Drug Formulary, 2023).

More recently, the addition of immune check point inhibitors (ICIs; pembrolizumab) to chemotherapy (cisplatin or carboplatin plus paclitaxel) with or without monoclonal

antibodies (bevacizumab), has led to clinically meaningful improvements in overall survival and progression-free survival (Monk et al., 2023) for those with cervical cancer. This has become the Canadian first-line standard of care for suitable patients diagnosed with metastatic, persistent, and recurrent cervical cancer.

Immune Checkpoint Inhibitors

Over the past 15 years, ICIs have radically changed cancer therapy. They have become a mainstay of treatment for many tumour types, proving significant clinical benefit with good patient tolerability (Weber et al., 2016). ICIs boost immune response by targeting receptors on the surface of T lymphocytes, which causes a reactivation of the patient's immune system to fight tumour cells (Shiravand et al., 2022). They block the checkpoint proteins from binding with partner proteins, which prevents the "off" signal" from being sent to the patients T lymphocytes and causing the cancer to evade the immune systems recognition and destruction of cancer cells (Tang et al., 2021).

These drugs are classified by their interactions with our immune system. Important interactions include the cytotoxic T-lymphocyte antigen programmed cell death protein-1(CTLA-4), programmed cell death protein-1(PD-1) and programmed cell death ligand-1(PDL-1).

PDL-1 is overexpressed in a high proportion of cervical cancer cells, making PDL-1 inhibition a target for treatment (Colombo et al., 2021). The Keynote -826 trial has shown the addition of pembrolizumab to chemotherapy (cisplatin or carboplatin plus paclitaxel) with or without bevacizumab has made statistically significant and clinically meaningful improvements in overall survival and progression-free survival.

Adverse effects

Despite numerous clinical benefits of adding the use of ICIs, there are a wide variety of side effects related to the mechanism of action and the 'ramping up' of the patient's immune system. These types of side effects are known as immune-related adverse effects (irAEs) that can range from mild to life threatening.

The incidence and timing of initial irAEs vary based on the class and dose of ICI, as well as single agent versus combination ICI therapy. Immune-related adverse effects and toxicities can occur in any organ of the body; however, gastrointestinal, pulmonary, endocrine, hepatic, and dermatologic are the most common areas of occurrence (Schneider et al., 2021). Typically, patients receiving anti-PD-1 or PD-L1 (this includes pembrolizumab) antibodies have a lower incidence of any-grade irAEs than those treated with anti-CTLA-4 agents (e.g., ipilimumab).

Unlike the predictable patterns and timelines associated with adverse effects of chemotherapy, irAEs vary in their onset and resolution and may occur anytime from a few weeks after treatment to several months after completion of treatment (Barber, 2019; see Figure 1). While toxicity is less common than with cytotoxic chemotherapy, early recognition and management can improve patient outcomes (Tang et al., 2021).

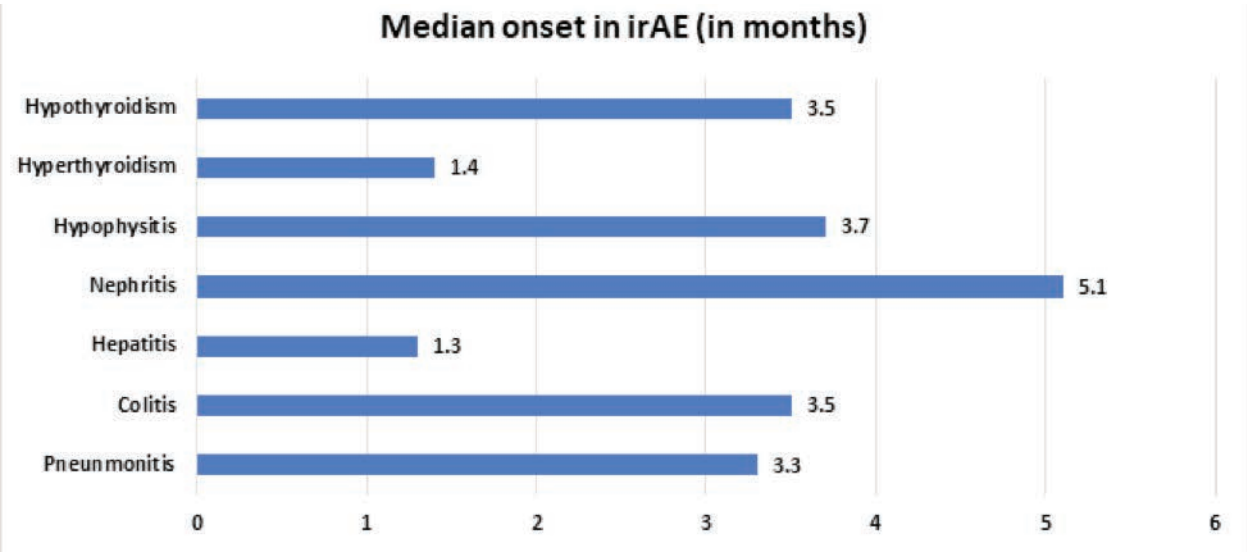
Nursing considerations

Although the combinations of ICI, chemotherapy, and targeted therapy have become the first-line treatment for metastatic cervical cancer, due to improved overall outcomes, these combinations make the recognition and management of toxicities more complex (Schneider et al., 2021). Clinicians must be aware of the potential for overlapping toxicities from combination therapies and attempt to distinguish the causative agent(s) for optimal management (Schneider et al., 2021).

It is recommended that nurses use a step-wise approach for these patients. This approach to irAE management was originally highlighted by Champiat et al. (2016) and is still widely used today (see Figure 2).

Figure 1

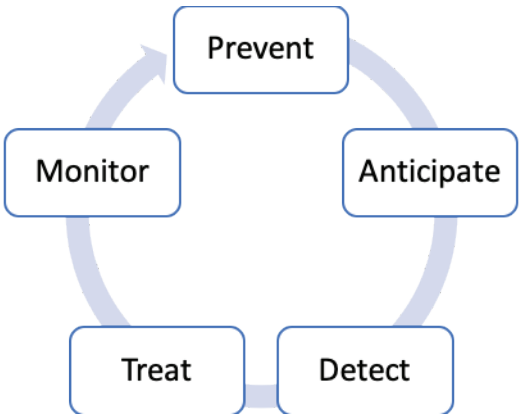
Pembrolizumab Median Onset of irAE



Note. Adapted from pembrolizumab drug monograph (2023) Cancer Care Ontario.

Figure 2

Five pillars of toxicity management



Note. Adapted from Five Pillars of Immuno-Oncology Toxicity Management by Champiat et al., 2016. Annals of Oncology 27, 559–574.

Prevent

It may not be possible to prevent irAEs and other adverse effects associated with combination therapy (ICI and chemotherapy), but the risk can be decreased by selecting patients appropriately. Schneider et al. (2021) identifies patients that have preexisting autoimmune disease, history of pneumonitis, or conditions that require systemic immunosuppressive therapy (i.e., organ transplant) as potentially poor candidates for ICI therapy.

The cancer care team must be aware and knowledgeable about the spectrum of toxicity associated with ICI alone and in combination therapy. Anti-PD1 / PD-L1 reported studies have drawn attention mainly to the adverse effects of colitis or pneumonitis because of their frequency and severity. However, nearly all organs can be affected by immune-related toxicities during or after completion of treatment (Champiat et al., 2016).

Anticipate

Prior to commencing any systemic therapy, including ICIs, the patient should undergo a comprehensive baseline assessment. This would include a thorough history and physical and laboratory tests including complete blood count, biochemistry, liver function tests, thyroid function tests, and cortisol levels. The oncology nurse must be knowledgeable about ICI (pembrolizumab) toxicities, as well as those from the chemotherapy with which it is combined (Monk et al., 2023). After initiation of treatment, the patient requires ongoing clinical assessment with routine clinical follow-up including bloodwork and other diagnostic tests, as required.

Detect

Patient and family education are an integral part of nursing practice. Educating and empowering patients with the ability to recognize signs of toxicity from their chemotherapy, as well as those related to their ICI is extremely important, yet this education can be complex. Patients should be informed that ICIs work differently than chemotherapy and that these therapies have unique side effects that can occur late in the treatment course or even after treatment has finished (Brahmer et al., 2018). Patient education on specific symptoms and signs of irAEs enables early intervention, potentially avoiding inpatient management and life-threatening adverse events (Schneider et al., 2021; NCCN 2023).

A recent study by Teixeira-Poit et al. (2023) confirmed that a multicomponent education strategy was effective in improving overall patient knowledge concerning ICI mechanisms of action, recognition of side effects, and what to do if side effects occurred. By using a multi-component strategy (e.g., written, verbal, and video), educators were able to capture different styles of adult learning. Research has shown that using the 'teach back' method is a highly effective method for teaching and learning. In the teach-back method, patient learners explain the health information they have been taught in their own words (Yen & Leasure, 2019). This allows the nurse to assess the patient's understanding of the information provided, especially when used in the healthcare setting (Talevski et al., 2020).

Treat

The American Society of Clinical Oncology, European Society of Medical Oncology, and the National Comprehensive Cancer Network have published and routinely updated numerous treatment guidelines for managing treatment-related side effects. The guidelines are available on the respective websites for these associations. Most of these guidelines contain similar recommendations and promote intervention for treatment based on the type and severity of the side effect. The interventions can range from temporarily stopping the drug, temporarily stopping the drug with administration of systemic corticosteroids, or permanent discontinuation of the ICI.

ICI's irAEs are graded by the Common Terminology Criteria for Adverse Events (CTCAE) from 1 (mild) to 4 (life threatening). Most irAEs are either Grade 1 (mild; asymptomatic or mildly symptomatic) or Grade 2 (moderate; moderately symptomatic, with some impact on daily living activities; Schneider et al., 2021).

Monitor

Oncology nurses must be aware of potential toxicities and attempt to distinguish the causative agent if appropriate management is to be initiated (Schneider et al., 2021). The National Comprehensive Cancer Network Management of Immunotherapy-Related Toxicities guidelines (2023) recommend regular monitoring of patients including physical exam and blood tests prior to each cycle of treatment. Completing bloodwork at regular intervals post-treatment is also recommended as irAEs can present after treatment has been completed.

The new first-line combination of pembrolizumab and chemotherapy (cisplatin or carboplatin plus paclitaxel) with or without bevacizumab offers a new strategy for effective management of metastatic, persistent, and recurrent cervical cancer. The addition of an ICI with chemotherapy presents new challenges for oncology nurses in the care and management of adverse effects for these patients.

CONCLUSION

Overall, cervical cancer treatment modalities, such as surgery, concomitant chemotherapy with radiation (external beam and internal brachytherapy), and systemic therapy including ICI often result in short-term and long-term side effects. Side effects include, but are not limited to, pain, nausea, fatigue, sexual dysfunction, irAEs, and peripheral neuropathy. The risk of these potential adverse effects guides treatment decisions when considering the stage of disease.

Oncology nurses are an integral part of the healthcare team and can decrease and manage toxicities and provide support. Through ongoing patient and family education, and the ability to anticipate, detect, treat, and monitor effects of treatment, nurses have the ability to improve adherence to treatment and, ultimately, enhance the cancer-patient journey for women diagnosed with cervical cancer.

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