REVIEW PAPER
Medycyna Paliatywna 2023; 15(3): 93–99
DOI: https://doi.org/10.5114/pm.2023.132018

The management of vaginal bleeding in advanced cervical cancer

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Abstract

Cervical cancer is the fourth most diagnosed malignancy worldwide. This narrative review aimed to assess various treatment methods for reducing or completely stopping vaginal bleeding, which is one of the most common and alarming complaints reported by women with cervical cancer. The treatment of bleeding depends on its intensity, potential causes (reversible and irreversible), stage of the disease, and prognosis. In advanced-stage patients receiving palliative care, interventional methods such as embolization or surgical ligation of internal iliac vessels, or epigastric or uterine arteries are usually not possible due to the patient's poor general condition. The treatment of choice is conservative therapy, which includes the performance of vaginal tamponade (usually using sterile gauze, haemostatic gauze, or cellulose sponges), the use of anti-haemorrhagic drugs (tranexamic acid, vitamin K), and, in selected clinical situations, palliative radiotherapy. The literature on the subject points to reports on the effectiveness of topical 4% formalin solution, Mohs paste, Monsel's solution, thrombin, or epinephrine in inhibiting vaginal bleeding. However, these are not supported by data from randomized clinical trials. Data available in databases on the alleviation of cervical vaginal bleeding are limited, so there is a need for further clinical research on this topic.

Key words: cervical cancer, prevention, HPV, palliative medicine, vaginal bleeding.

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INTRODUCTION

Cervical cancer is a term used to describe tumours that can develop in the lower end of the womb (uterus) [1]. The cervical canal of the cervix (neck of the womb) is lined with mucous membrane with glands producing a thick fluid, which acts as a barrier, preventing pathogens from entering higher structures of the genital tract (uterus, fallopian tubes, ovaries) [1]. The human papillomavirus (HPV) is one of the most common viral infections of the reproductive tract of sexually active individuals, both male and female, which occurs either through skin-to-skin or mucosa-to-mucosa contact [2]. Although HPV infections clear up spontaneously, there is a risk that these infections may further progress into precancerous and cancerous lesions [3, 4]; most precancerous lesions lead to cervical cancer [5].

This narrative review aims to assess various treatment methods for reducing or stopping vaginal bleeding completely, which is one of the most common and alarming complaints reported by women with cervical cancer. It also briefly presents methods of prevention, diagnosis, and treatment of cervical cancer.

EPIDEMIOLOGY OF CERVICAL CANCER

Cervical cancer is the fourth most diagnosed malignancy, responsible for approximately 604,000 new cases and 342,000 deaths annually worldwide [3]. Roughly 3000 patients are newly diagnosed each year in Poland, and according to the International Agency for Research on Cancer, its age-standard mortality rate of 4.9 deaths for every 100,000 women/year gives Poland the seventh highest mortality rate in Europe [6, 7]. The geographical area plays a crucial role in the incidence rate and stage of cervical cancer at the moment of diagnosis [3, 8], which are highly dependent on access to screening programs allowing early identification of precancerous lesions. Because low- and middle-income countries have restricted access to these preventative measures, cervical cancer is usually diagnosed at an advanced stage in these countries when evident symptoms, such as vaginal bleeding, appear [3, 8, 9]. Furthermore, developing countries have limited access to anticancer therapy (oncological surgery, chemotherapy, and radiotherapy – RT), which may result in a higher mortality rate [3]. Some women, specifically those diag-

Table 1. International Federation of Gynaecology and Obstetrics staging of cervical carcinoma [4]

Stage	Description
I	Carcinoma confined to the cervix (extension to the uterine corpus should be disregarded)
	IA – carcinoma diagnosed only by microscope, with a maximum depth of invasion ≤ 5 mm IA1 – measured invasion of stroma ≤ 3 mm in depth IA2 – measured invasion of stroma > 3 mm and ≤ 5 mm in depth
	IB – measured deepest invasion of > 5 mm, with lesion limited to the cervix IB1 – lesion > 5 mm deep and ≤ 2 cm in largest dimension IB2 – lesion > 2 and ≤ 4 cm in largest dimension IB3 – lesion > 4 cm in largest dimension
II	Extension beyond the uterus but not to the pelvic wall or to the lower third of the vagina
	IIA – limited to the upper 2/3 of the vagina without parametrial involvement IIA1 – lesion ≤ 4 cm in largest dimension IIA2 – lesion > 4 cm in largest dimension IIB – parametrial involvement but not up to the pelvic wall
III	Extension to the pelvic wall and/or involves the lower third of the vagina and/or causes hydronephrosis or a non-functioning kidney and/or involves pelvic and/or para-aortic lymph nodes
	IIIA – extension to the lower third of the vaginal but not to the pelvic wall IIIB – extension to the pelvic wall and/or causes hydronephrosis or a non-functioning kidney (unless known to be due to another cause) IIIC – involves pelvic and/or para-aortic lymph nodes, regardless of tumour size and extent IIIC1 – only metastasis to pelvic lymph nodes IIIC2 – metastasis to para-aortic lymph nodes
IV	Extension beyond the true pelvis or biopsy-proven involvement of the bladder or rectal mucosa
	IVA – spread to adjacent pelvic organs IVB – spread to distant organs

nosed at an advanced stage, can be qualified only for palliative care [9, 10] at the time of the diagnosis.

The incidence risk of cervical cancer increases after the age of 25 years. A study performed in 2018 stated that women living in high-income countries manifest with cervical cancer at an earlier age, typically around the age of 40 years, while in low-income countries they were diagnosed at a later age, ranging 50–69 years [11]. However, it has been stated that the average age of diagnosis ranges 35–44 years globally [11]. Although younger women generally better tolerate treatment and are better candidates for aggressive treatment, as opposed to women of advanced age, they may experience late radiation complications that can significantly negatively impact their quality of life (QoL) [12]. All types of cancer patients of advanced age often have a worse prognosis regardless of comorbidities, histologic type, and stage of disease [11].

CERVICAL CANCER – RISK FACTORS, PREVENTION, AND TREATMENT

Several risk factors are linked to the increase in the prevalence of cervical cancer. These include initiating sexual activity under the age of 16 years, having multiple sexual partners and infrequent condom use, prolonged use (more than 5 years) of oral contraceptive pills, having a weakened immune system (including being HIV positive), low socioeconomic status, and smoking [13]. In addition to these risk factors, it is valid to note that some researchers reported a massive gap in knowledge about the risk factors in the general population [14, 15], which may result in delayed diagnosis and treatment because women are unaware of how the disease presents itself [16] or whether they are at risk.

Identifying cervical cancer at an early, curable stage can be achievable with the aid of the 3 elements of prevention recommended by the World Health Organization (WHO). It encompasses a global strategy that can help accelerate the elimination of cervical cancer and search for the most common aetiology, i.e. HPV. Primary prevention includes vaccination against the oncogenic types of HPV in young people who have not started sexual intercourse. Secondary prevention involves regular screenings for cervical cancer through Papanicolaou smears. Tertiary prophylaxis includes measures to halt the progression of the disease and reduce complications through the effective treatment of pre-cancerous and cancerous lesions and early palliative care [8, 15, 17]. Men and women are exposed to an HPV infection over their lifetime, the majority of which will resolve spontaneously within the following 2 years, without any need for intervention [18]. However, there is a risk that this infection will progress into pre-cancerous and cancerous lesions [3, 4].

Before cervical cancer spreads to distant organs of the body, it develops locally within the pelvis, either to, or without the involvement of, regional

Table 2. Symptoms of cervical cancer [10, 21]

Early-onset symptoms	Late-onset symptoms
Early onset, meaning the cancer is situated within the cervix (stage I–IIa according to FIGO classification)	Late onset, meaning the cancer has spread beyond the cervix and to other parts of the body (stage IIb–IVb according to FIGO classification)
Asymptomatic (no symptoms) Unusual vaginal bleeding: • post-coital bleeding • bleeding post menopause • intermenstrual bleeding • menses which last longer/heavier than usual Vaginal discharge containing blood/unpleasant odour Pelvic pain Painful intercourse	Early-onset symptoms Difficulties with passing stool Rectal bleeding while defecating Difficulties with passing urine Blood present in the urine Abdominal pain Overall fatigue, weight loss, and loss of appetite

FIGO – International Federation of Gynaecology and Obstetrics

lymph nodes, where cure is still possible. According to the International Federation of Gynaecology and Obstetrics classification (Table 1), stages I–IIa can be treated effectively with radical surgery. The addition of postoperative adjuvant RT is considered in cases with a high risk of recurrence [9, 12]. Once the cancer metastasizes to distant organs (stages IIb–IVb), chemotherapy, external beam radiotherapy (XRT), and brachytherapy (BT) are the main treatment options [19]; surgical measures are typically avoided in these stages [9]. The Eastern Cooperative Oncology Group performance scale, also called the WHO or Zubrod score, is used to qualify cancer patients for specific types of oncological treatment. Therefore, a woman with a reasonable score may also benefit from surgical measures. Moreover, women of younger age may experience a more aggressive approach: surgery, XRT + BT, surgery + BT, surgery + XRT, or surgery + XRT + BT. Whereas women of more advanced age may receive a less aggressive approach: XRT alone or BT alone [11] – and at each stage, the addition of palliative treatment is always possible.

Palliative care is an approach that aims to improve the QoL of patients suffering from life-threatening diseases, from early to late stage, by alleviating associated symptoms (such as nausea, vomiting, fatigue, and pain) and providing psychological, social, and spiritual support [9]. Palliative care not only focuses on the patient but also supports caregivers' psychological and overall well-being [8]. The palliative care approach is of particular importance in low-income countries, where there is not only a gap in knowledge but also a lack of access to early and late prevention, so cervical cancers diagnosed at their early stage result in rapid disease progression because of limited access to early diagnosis and anticancer treatment [8, 20]. However, in these countries, palliative care should be universally accessible [15]. On the other hand, home palliative care in high-income countries is an immense asset in the late stages of cervical cancer. It decreases the risk of unnecessary hospital visits, ensuring patients' symptomatic relief and good QoL at their homes [8]. For patients with advanced cancer, hospitalization relates to an increased risk of hospital-acquired infections, potentially resulting in an increased risk of death.

SYMPTOMS OF CERVICAL CANCER

Cervical cancer can be either asymptomatic or presented with unspecific symptoms, making it difficult to detect. For this reason, cervical cancer is often diagnosed in an advanced stage, when unambiguous clinical symptoms, such as abnormal vaginal bleeding, occur. Symptoms of cervical cancer can be distinguished into early- and late-onset categories, as presented in Table 2 [10, 21].

Data from the currently available literature indicates that the prevalence of vaginal bleeding in women with cervical cancer ranges 0.7–100% [9]. With vaginal bleeding, challenges frequently emanate and may lead to multiple consequences, such as anaemia from recurrent episodes, potentially requiring a blood transfusion, or they may even be life-threatening due to primary haemorrhage [9]. Specifically in advanced-stage cancer, massive vaginal bleedings are the immediate cause of death in about 6% of women [8]. There are a variety of interventions that can be used for vaginal bleeding in a palliative care setting. Their effectiveness varies and depends on the patient's general condition.

In a retrospective study performed in 2015, out of 72 patients with cervical cancer, 62 (92%) women declared that pain was the most common complaint [10] (particularly in those with advanced cervical cancer) that required palliative interventions. Because the severity of pain increases as the development of cancer progresses, these women often reported experiencing pain in more than 2 areas of the body with an overall score of 4 on a pain scale of 0–5 (0 being no pain; 5 being severe pain) and required the administration of opioids. As time progressed, a consequent study that was conducted in 2021 revealed that vaginal bleeding

was also commonly reported, with a high prevalence of 89% [16]. Although intermenstrual and post-coital bleedings are common symptoms of cervical cancer, they may also be associated with benign conditions such as polyps, uterine fibroids, ovulatory or endometrial-related disorders, birth control, sexually transmitted infections, or trauma [22, 23].

Postmenopausal bleeding, however, is a symptom of concern because it requires extensive investigation to exclude potential malignancy [22]. In women experiencing heavy bleeding (menorrhagia) with concomitant pain, significantly reduced QoL is observed, which shows how the aforementioned symptoms can impact overall physical, social, and psychological well-being [23]. In a recent study analysing the QoL in women with heavy menstrual bleeding (HMB), the authors of the study developed a reliable tool, the "PERIOD-QOL" online questionnaire, assessing QoL in this group of patients. The study enlightened the significance of HMB and revealed that despite experiencing these stressful symptoms, women can still be reluctant to seek medical help, worrying that people might think they are making an unnecessary fuss about a natural part of womanhood [23].

Pain is considered one of the most common symptoms of advanced cervical cancer (for example, in the study conducted in Malawi by Bates *et al*. [10], the percentage of patients with pain reached almost 96%), usually presenting at either moderate or severe levels. The pelvis is richly innervated by the sacral plexus and inferior gastric plexus. Therefore, neuropathic pain, frequently observed in cervical cancer, is usually a consequence of infiltration of nerve endings and pelvic bones [15, 24]. Moreover, neuropathic pain may also arise as a consequence of pelvic nerve injury from surgery, as an adverse effect of commonly used chemotherapeutics (such as paclitaxel and cisplatin), or RT. This specific type of pain is much more demanding than nociceptive pain. The opioid agonists in monotherapy may not be sufficient in this case; gabapentinoids or serotonin-norepinephrine reuptake inhibitors are usually applied as adjuvants to enhance the analgesic effect [8, 21]. Inadequately treated pain leads to significant obstacles, such as restriction in patients' mobility and the dependency on caregivers to perform simple tasks [15]. Pain intensity should be assessed regularly because its degree and character may change over time as the cancer progresses. Such a course of action allows for rapid and adequate modifications of treatment if pain intensifies. Primitively, pain should be assessed several times a day, and once it stabilizes, it should be monitored regularly.

MANAGEMENT OF VAGINAL BLEEDING

According to the American College of Obstetricians and Gynecologists, the initial evaluation of a patient with vaginal haemorrhage should include a prompt assessment for signs of hypovolaemia and potential haemodynamic instability. The evaluation process should be conducted in 3 steps:

- rapidly assessing the severity of the patient's condition,
- determining the most probable aetiology of bleeding,
- choosing the most appropriate treatment for the patient [25].

In advanced and metastatic cervical cancer, the probability of vaginal bleeding results in nearly 100% of patients. Patients are usually in poor general condition at this stage of the disease. Therefore, aggressive surgical treatment is not the treatment of choice. The use of vaginal tamponades, antihemorrhagic drugs, or palliative RT are the preferred conservative treatment options.

LOCAL TREATMENT OF VAGINAL BLEEDING

The standard treatment of vaginal bleeding should start with a simple first-aid approach that consists of the following:

- insertion of 2 large-bore intravenous lines,
- initiation of fluid resuscitation,
- reversal of coexisting coagulation disorders.

The patient should be positioned in the dorsal-sacral (lithotomy) position, exposing the superior aspect of the vagina with a speculum. Unfortunately, hospice settings are usually not supplied with the appropriate equipment, such as a gynaecological examination chair on which to place the bleeding woman in the above position; the transvaginal examination is usually performed in the patient's bed. Moreover, a gynaecological speculum is a very useful tool, especially in the case of vaginal bleeding, but unfortunately it is not an essential piece of equipment in palliative care units.

Vaginal packing (tamponade) is the treatment of choice aimed at absorbing blood and applying pressure to the bleeding area. To insert a tamponade, the patient should be positioned in the dorsal-sacral (lithotomy) position with their hips and knees flexed and with their knees falling to the sides, exposing the superior aspect of the vagina with a speculum. Simple rolled gauze, haemostatic gauze, or haemostatic cellulose sponges should be tightly packed into the upper part of the vagina to apply even local pressure, halting the bleeding [9]. Sedation or short-acting general anaesthesia for the vaginal tamponade procedure should be considered [9, 16]. It is significant to note that the vaginal packing should be removed within 24–36 hours.

Because the urethra lies close to the distal vagina, to some extent, this vaginal packing applies pressure

to the urethra as well, resulting in difficulties in urination and even urinary retention. Therefore, the placement of a tamponade is an indication of bladder catheterization [9, 16]. In addition, patients' mobility should be restricted to enhance the efficacy of the packing. Because patients with solid tumours, such as cervical cancer, are usually immunocompromised and are more prone to infections, it is recommended that broad-spectrum antibiotics be prophylactically administered to all patients with the vaginal tamponade, to prevent infections associated with the presence of a foreign body in the vagina, including toxic shock syndrome. Both aerobic and anaerobic bacteria should be covered by antibiotics [9, 26]. Metronidazole applied intravaginally twice daily may be added to the treatment regime, acting not only to prevent infection but also to help eliminate or reduce malodorous vaginal discharge, which may cause patients to isolate themselves from social contact [8, 24].

Another option before inserting the gauze rolls into the vagina is pre-soaking them with 4% formalin. Formalin, an aqueous formaldehyde solution, acts as a haemostatic agent by initiating a chemical cauterization and reducing bleeding from small blood vessels [9]. Due to its antimicrobial properties, 4% formalin may prevent infections related to the presence of a foreign body in the vagina. Moreover, it is well-tolerated, and no toxic adverse effects have been reported at low concentrations [9].

Yanazume *et al*. [27] reported the clinical usefulness of Moh's paste for genital bleeding from the cervix or vaginal stump in 8 patients with recurrent gynaecological cancer. Moh's paste, made up of a 20% mixture of zinc chloride paste, was first used in the 1930s by Frederic F. Mohs for the chemical fixation of a cutaneous tumour [28]. Moh's paste, applied directly to the bleeding tumour, causes tissue necrosis, and therefore it should not be applied to healthy tissues. In the study of Yanazume *et al*. [19] Moh's paste was applied directly to the most active bleeding region of the tumour with a large pledget and soft pressure applied for a few minutes. Twenty-four hours later, the pledget was removed, and as much paste as possible was wiped from the tumour surface. After one application of Moh's paste, the procedure may be repeated in patients with recurrent genital bleeding. The possibility of attaining an antihemorrhagic effect can be continued for 5 days to one year (in 3 patients it was continued for 3 months or more); none of the 8 study participants died due to genital bleeding [19]. The literature also contains data on the effectiveness of Monsel's solution (20% ferric subsulphate) – a haemostatic agent leading to tissue necrosis and eschar formation, thus enhancing thrombus formation and haemostasis [9]. Monsel's solution can be applied directly to the bleeding cervix or by a gauze pack.

When the patient continues to bleed profusely, the tamponade should be removed and replaced with a new one. New packing can be coated with 5000 U of thrombin in 5cc of saline placed on the end of the gauze and placed in the closest proximity to the cervix [9]. A ready-made bandage soaked in antihaemorrhagic agents can also be applied locally to stop bleeding. An example of ready-made dressings is QuikClot Combat gauze impregnated with kaolin, an inorganic mineral that activates Factor XII, and chitosan-based dressing ChitoGauze XR Pro. Moreover, dressings saturated in 1 : 1000 adrenaline solution are applied locally in chronic low-pressure blood oozing [29].

The authors of this publication are aware of the fact that findings from currently available research in databases have some limitations, including the small number of enrolled subjects and heterogeneous cancer types. However, due to the lack of clear recommendations regarding the management of vaginal bleeding, the following data may be used in everyday clinical practice in cases of bleeding that are refractory to treatment.

SYSTEMIC TREATMENT OF VAGINAL BLEEDING

Systemic options for treating vaginal bleeding include the use of tranexamic acid (TXA) – a fibrinolytic inhibitor that not only reduces the conversion of plasminogen to plasmin by antagonizing the activation of plasminogen by fastening to its kringle enzymatic domain but also antagonizes the actions of plasmin directly [9]. TXA is administered orally or intravenously 3 times a day at a daily dose of 3 g (1 g t.i.d p.o.) when administered per os, and 10 mg/kg body weight (max. dose 600 mg/daily i.v.) respectively with minimal side effects observed [9, 30]. Tranexamic acid is widely used to treat haemorrhages and prevent recurrent bleeding. Moreover, it decreases the need for a blood transfusion [9, 30]. Tranexamic acid may be solely used to palliate mild to severe bleeding or in addition to the aforementioned local treatment [9, 16, 30]. Before its administration, it is crucial to estimate the patient's age, weight, and kidney function [31] because the dose is calculated based on these 3 factors. Contraindications include acquired impaired colour vision and current thrombotic or thromboembolic disease; the drug should be applied with caution in patients with a history of thrombosis [32]. Unfortunately, there are a lack of data from high-quality clinical trials that confirm the effectiveness of TXA in vaginal bleeding in the course of cervical cancer.

Vitamin K is used in the management of bleeding caused by an overdose of anticoagulants derived from coumarin or in patients with deficiencies

of vitamin K-dependent clotting factors (factors II, VII, IX, X) [33]. In case of severe bleeding, including life-threatening bleeding, anticoagulants should be discontinued, and vitamin K should be administered at a dose 10–20 mg in an infusion (after diluting in 100 ml of 0.9% solution of sodium chloride) or slowly intravenously. Prothrombin time should be determined 3 hours after vitamin K administration, and the dose of vitamin K should be repeated when it is prolonged. However, doses greater than 40 mg daily should not be used. In less severe bleeding, vitamin K can be administered orally.

Some authors reported the effective use of human recombinant activated factor VII in bleeding from endometrial and vaginal malignant tumours in 2 patients without pre-existing coagulopathy, stating that it can be an important and effective drug in severe bleeding in gynaecological oncology [34].

PALLIATIVE RADIOTHERAPY

Palliative-dose RT with a standard curative treatment dose 1.8–2.0 Gy in a single fraction is considered an effective method of alleviating vaginal bleeding in cervical cancer [35]. In the setting of palliative care for haemostatic purposes, the variety of treatment regimens, including single treatments of 8–10 Gy, immediate courses of 4–8 Gy given in 3–5 treatments, or longer courses of 30–45 Gy in 10–15 treatments are used, and no treatment scheme has been proven to be more effective than another [33]. If the patient is haemodynamically stable enough for transport to the radiation department, radiation therapy to palliate bleeding can be delivered in a small number of treatments and can be effective within 24–48 hours of the delivery of the first dose [33]. Palliative doses of RT applied to the bleeding cervix reduce the necessity for additional blood transfusions [16]. In a retrospective study conducted in 2021, it was found that in early cervical cancer, delivering a single dose of 8 Gy, 0.5 cm from the tumour surface, showed similar effects in bleeding control in comparison to the North American guidelines with a recommended 2 regimens of 5 Gy [16]. Because there is a risk of developing late, severe radiation toxicity (typically seen 9–10 months after treatment [24]), short courses of hypofractionated RT are given at a range of 8–10 Gy for 1–3 fractions to patients with advanced stage disease and a limited life expectancy, with effective results to control both vaginal bleeding and discharge [36]. A retrospective imaging study conducted in 2021 reported that most patients who experienced late radiation effects (≥ 6 months post adjuvant RT) in cervical cancer, were minor, asymptomatic, and were only evident on computed tomography, positron emission tomography/computed tomography, or magnetic resonance imaging [12]. The most frequent late RT complications were typically situated in the urological or gastrointestinal tracts, varying from mild cystitis to ileus, respectively. The most common complications noted in this study were cystitis and mild proctocolitis/enteritis [12]. However, palliative care patients typically suffer from hydronephrosis, entero-ureteral fistulas, and ileus.

END-OF-LIFE CARE FOR PATIENTS WITH VAGINAL BLEEDING

In about 6% of women with cervical cancer, massive vaginal bleeding is the direct cause of death [37]. In this situation, when excessive vaginal bleeding occurs at the end of life, the application of vaginal tamponade and antihemorrhagic drugs are the treatments of choice. However, anxiolytics and analgesics are no less important in reducing the suffering and distress of dying patients. Both the patient and caregivers should be provided with psychological and supportive care in this stressful time [9].

CHALLENGES OF PSYCHOLOGICAL CARE

Psychological distress is experienced among many women with cervical cancer. Specifically, for those living in low- and middle-income countries, being diagnosed at an advanced stage is overwhelming, and the prevalence of anxiety and depression is high. Also, the fear of losing a loved one, and consequently potentially experiencing financial difficulties due to a loss of income, caregiving burden, and prolonged grief after the death of the patient, are some of the thoughts of the family members of patients with this unfortunate diagnosis [15, 16]. Fortunately, both pharmacological and nonpharmacological measures can be delivered in this case. Pharmacological interventions include providing anxiolytics and antidepressants to alleviate anxiety and depression. Psychotherapy, psychoeducation, and music and art therapy are examples of nonpharmacological approaches from which both patients and their family members may benefit [8].

CONCLUSIONS

Cervical cancer is the fourth most diagnosed malignancy worldwide. Vaginal bleeding is one of the most common and distressing symptoms of cervical cancer, occurring with a frequency ranging from 0.7% to almost 100% in advanced stages of disease. There are a variety of interventions that might be used to control bleeding, depending on

the patient's overall condition. In palliative care patients, use of conservative therapy, such as vaginal tamponade, antihemorrhagic drugs, or palliative RT, is the treatment of choice.

Regardless of all recommendations, it is important to implement the simplest measures of educating and spreading awareness on what exactly HPV is, what can be done to decrease its transmission, and the significance of regularly attending gynaecological check-ups.

The authors declare no conflict of interest.

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