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NON-STANDARD STRATEGIES IN THE TREATMENT OF ADVANCED CERVICAL CANCER: A CASE SERIES

Background. Cervical cancer (CC) continues to be the leading cancer pathology affecting women of both young and older ages. In the advanced stages of CC, the choice of treatment typically favors chemoradiotherapy. However, in a number of cases, radical surgery may be the only effective treatment. This issue requires further analysis. **Materials and Methods.** Five selected cases of the advanced CC (stages IIa–IVa) that required non-standard treatment are presented. **Results.** In all presented cases, the radical surgical treatment had an undeniable immediate curative effect. On follow-up, two patients are alive without any evidence of the disease; two patients died from disease progression and one patient is still receiving treatment for bone recurrence. **Conclusions.** Despite the fact that in most cases of advanced stages of CC, chemoradiotherapy is effectively used, in some selected cases, surgery may be leading and effective if the operation is performed in a radical manner. Important in this regard are the clinical experience, high level of surgical skills, presence of a multidisciplinary team, and the technical equipment of the medical center for performing such operations.

Keywords: advanced cervical cancer, radical surgical treatment, symptomatic retroperitoneal lymphocyst, pelvic exenteration.

Cervical cancer (CC) remains one of the leading gynecological malignancies, affecting women of both young and old age. At the advanced stages, the choice of treatment tactics is decided in favor of chemoradiotherapy. However, in a number of selected cases, radical surgical treatment may be the only effective choice.

Several reports explored the data on the outcomes of radical surgical treatment in cases of advanced CC. Chakrabarti et al. [1] analyzed a large

cohort of women with locally advanced CC who, after receiving chemoradiotherapy as first-line treatment, were diagnosed with residual disease in the cervix, and found no evidence for or against debulking hysterectomy followed by chemoradiotherapy compared with chemoradiotherapy alone for FIGO stage IB3/II CC. In a systematic review of studies on the role of salvage surgery for persistent or recurrent disease in patients with locally advanced CC, who had undergone radical chemora-

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Fig. 1. Colpophotography of the ectocervix before surgery: the tumor occupies up to 25% of the ectocervix surface

diation therapy, Conte et al. [2] stated that the adequate assessment of possible benefits is difficult due to the heterogeneity between the designs and results of different studies. They suggested that further studies on appropriately selected patient populations are needed. Saemathong and Chaowawanit [3] investigated complications arising from pelvic and para-aortic lymphadenectomy in gynecologic oncology, including CC surgery, and noted that, although complications were reported in nearly half of the cases, the rate of severe complications was low. In particular, the rate of symptomatic lymphocysts was 6%, and this complication was observed in the extended postoperative period.

In this study, we aimed to present and discuss several selected cases of advanced CC from our practice, in which the radical surgical treatment seemed to be acceptable.

Materials and Methods

5 non-standard surgical treatment cases of patients with advanced CC (stages IIa—IVa) were selected among a series of the cases operated at the Scientific and Clinical Department of Female Reproductive Neoplasms of the National Cancer Institute (Ukraine) in 2021—2025. The cases were depersonalized, and the patients' consents to use their medical data for scientific purposes were obtained. At the preoperative stage, all patients were examined according to generally accepted standards, and at the observation stage after treatment, they were examined by a gynecologist-oncologist from the outpatient department of the National Cancer Institute.

Results

We present a series of the advanced CC cases with surgical treatment, in which a radical surgical treatment had undeniable proximate curative effect.

Case 1. Patient K.N., 63 years old, diagnosed with CC stage IIb cT2bN0M0 G₂ (Fig. 1). The patient began experiencing postmenopausal bleeding and aching pain in the lower abdomen in August 2024. In January 2025, curettage of the uterus and cervical canal was performed and, according to morphological review results, in the examined material of endometrial scraping and cervical biopsy, the growth of adenocarcinoma with mucus production according to the type of mucinous adenocarcinoma G₂ was confirmed. MRI of the pelvis and abdomen with intravenous contrast enhancement suspected the pelvic lymph node involvement and contact invasion of the parametrium (Fig. 2, 3). By ultrasound, a cervical-isthmic node was detected on the posterior wall, to which the tumor process had spread, as well as an enlarged uterus with a dilated cavity filled with thick liquid contents (Fig. 4, 5).

On 03/12/2025, the surgery was performed in the following scope: Lower-midline laparotomy. Radical panhysterectomy type C2. Pelvic 2-sided lymphadenectomy (Fig. 6, 7).

The pathohistological report stated the following: Moderately differentiated endocervical adenocarcinoma of the cervix, Silva pattern C, with the presence of extensive fields of mucin, which is characteristic of the mucinous subtype of endocervical adenocarcinoma, infiltrates the entire thickness of the cervix, spreads to the adjacent subserous leiomyoma and fatty tissue (parametrium), the isthmus of the uterine body, with diffuse lymphovascular, focal venous and perineural invasion, and necrosis of tumor tissue. Endometrium without signs of functional activity with diffuse pronounced lymphocytic infiltration, corresponding to chronic active endometritis, with massive hemorrhages. Sclerosis of the fallopian tube villi. The ovaries with fibroids, serous cysts, and foci of inactive endometriosis. 10 examined regional lymph nodes and the vaginal resection margin without signs of tumor growth. pT2bN0M0 LV1 Pn1 R0 (Fig. 8—10).

In the postoperative period, the patient received a course of combined radiotherapy against the background of concurrent platinum-contain-

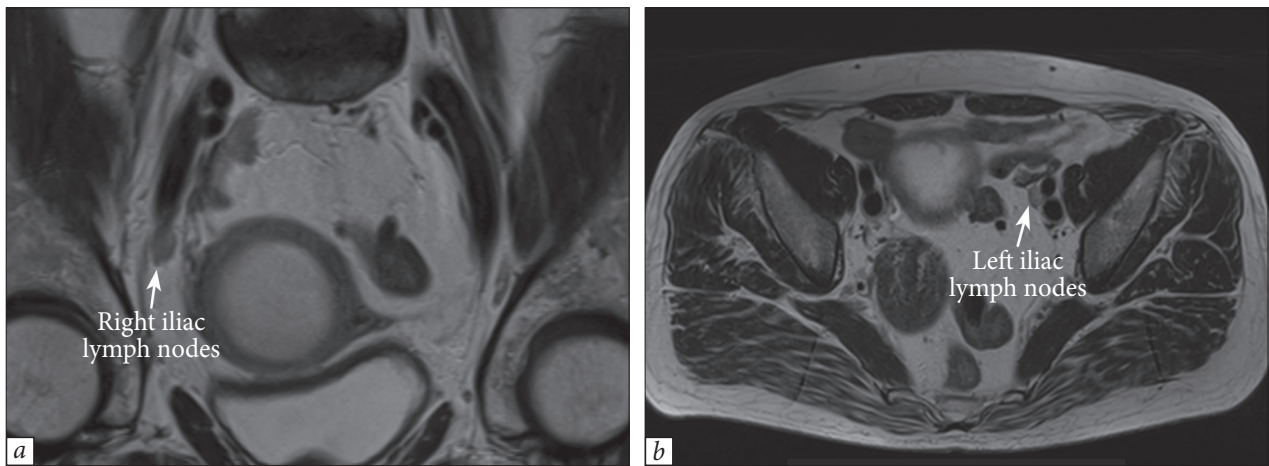


Fig. 2. External iliac lymph nodes on both sides are spherically transformed without clear contours, suspicious for metastatic lesion: *a* — T2WI-cor; *b* — T2WI-axial

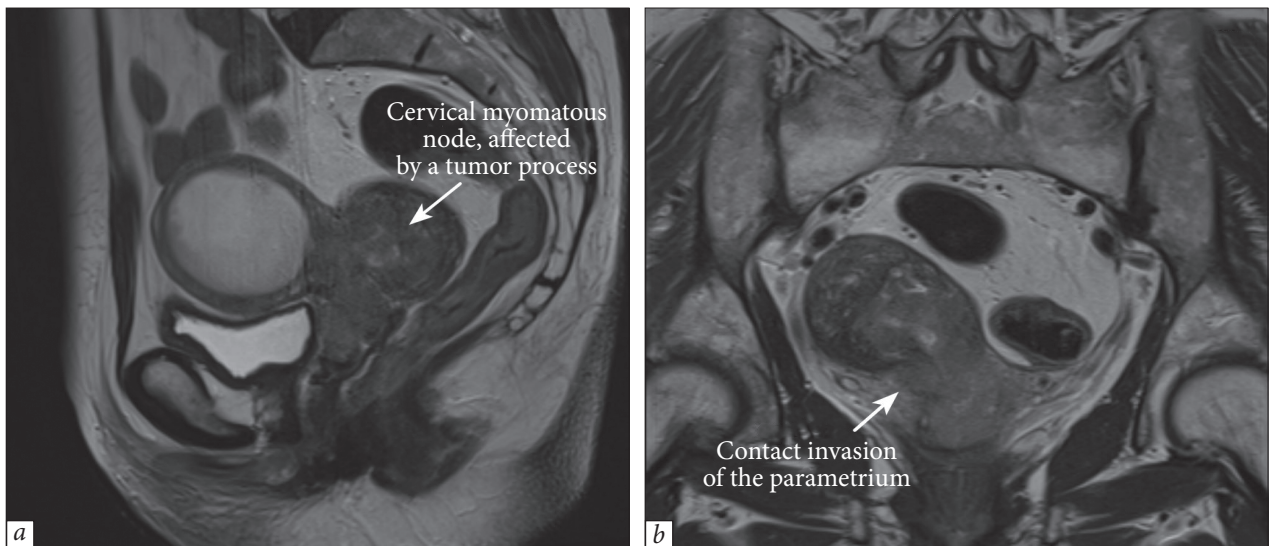


Fig. 3. T2-WI on sagittal (*a*) and coronal scans (*b*) shows an enlarged cervix with a cervical myomatous node, affected by the tumor spreading endophytically along the cervical canal to the isthmus of the uterus and the cervical myomatous node, with contact invasion of the parametrium

ning chemotherapy — cisplatin 40 mg/m², weekly, completed in June 2025. The patient is under observation currently with no signs of the disease recurrence.

Case 2. Patient S.E., 42 years old, diagnosed with CC stage IIa, cT2aNxM0 G₃. In August, 2023, a cervical biopsy was performed. According to pathohistological report, squamous non-keratinized cervical carcinoma G₃ was detected. The patient received 3 cycles of neoadjuvant chemotherapy according to the paclitaxel + carboplatin + bevacizumab regimen. By MRI of the pelvis and abdominal cavity in October 2023, pronounced positive dynamics and partial regression of the tumor were evident.

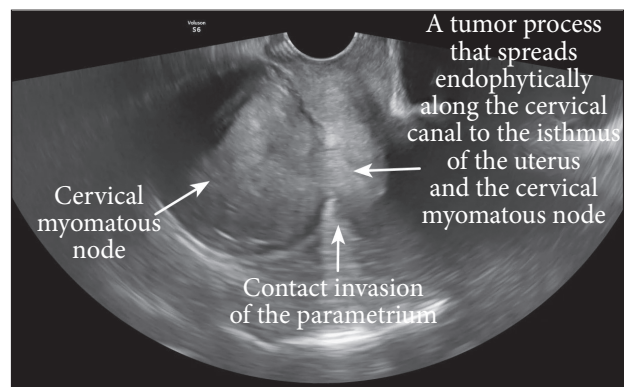


Fig. 4. The tumor spreads endophytically along the cervical canal from the external opening to the isthmus and to the lower segment of the uterine body, grows into the cervical myomatous node, and invades the parametrium at the level of the isthmus

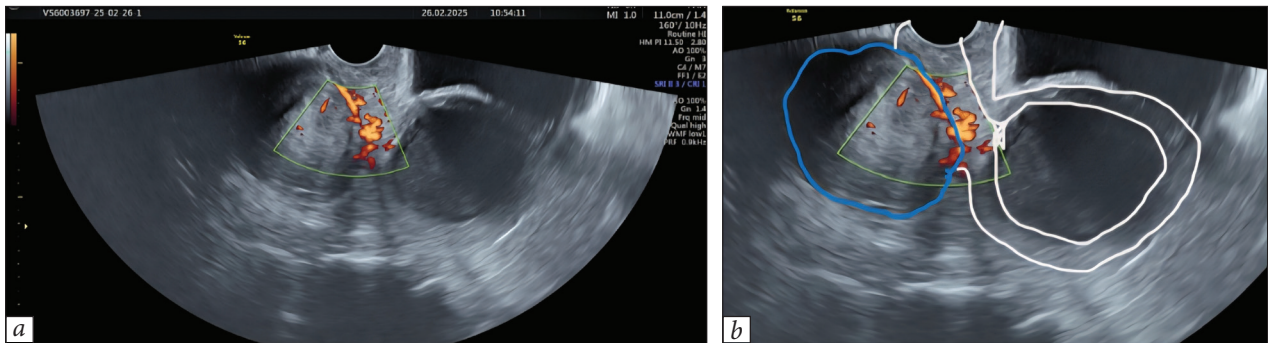


Fig. 5. Ultrasound of the uterus (a) and schematic image (b): a cervical myomatous node on the posterior wall of the cervix (circled in blue), the uterine cavity is dilated and filled with the liquid content. The increased atypical vascularization of the uterus is noted

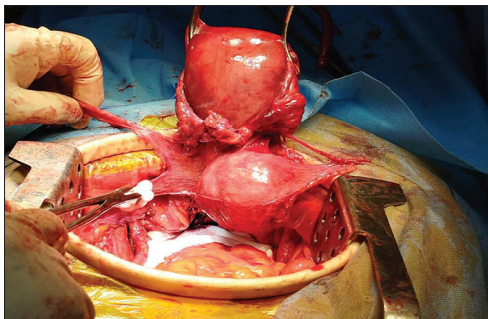


Fig. 6. A resected specimen with a cervical node

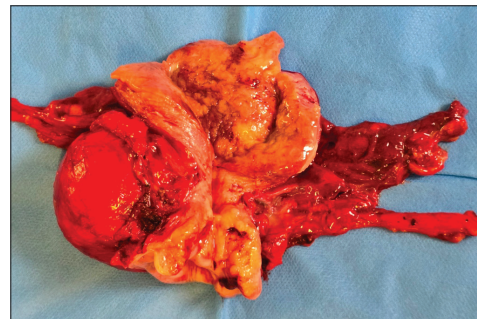


Fig. 7. A section of the resected specimen

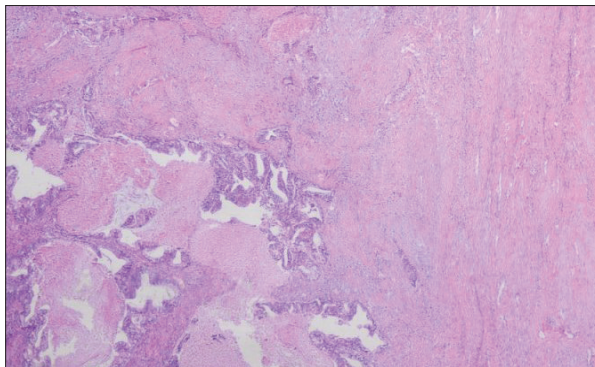


Fig. 8. Transition of the tumor to a cervical leiomyoma. $\times 100$ H&E staining

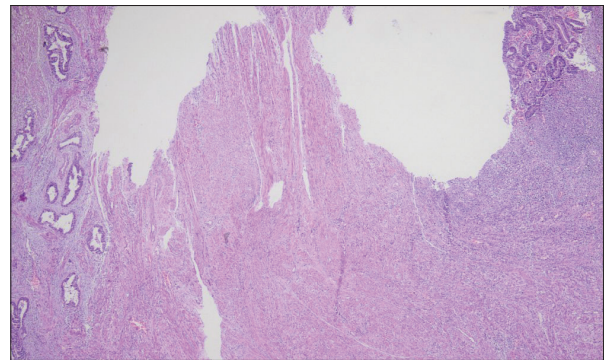


Fig. 9. Tumor transition to the isthmus of the uterus. $\times 50$ H&E staining

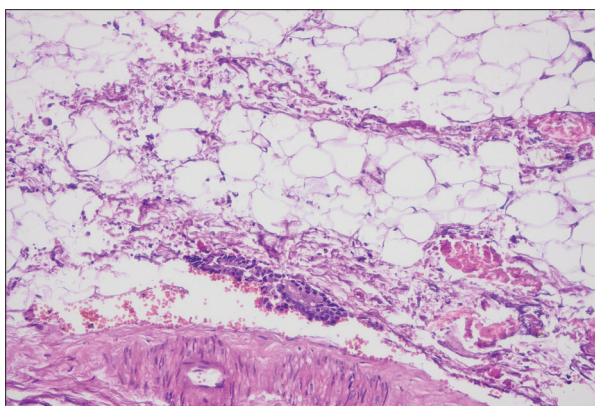


Fig. 10. Transition of the tumor to the fatty tissue of the parametrium. $\times 100$ H&E staining

In November 2023, surgery was performed in the following scope: Radical hysterectomy type C2. Bilateral pelvic and para-aortic lymphadenectomy. The pathohistological report stated the following: In the examined areas of the cervical tissue with the transition to the cervical canal, focal growths of poorly differentiated carcinoma with areas of solid and solid-polypous growth types after chemotherapy, with infiltration up to half of the wall thickness, and the presence of lymphovascular and perineural invasion are revealed. Morphologically, it is difficult to determine the type of carcinoma: poorly differentiated squa-

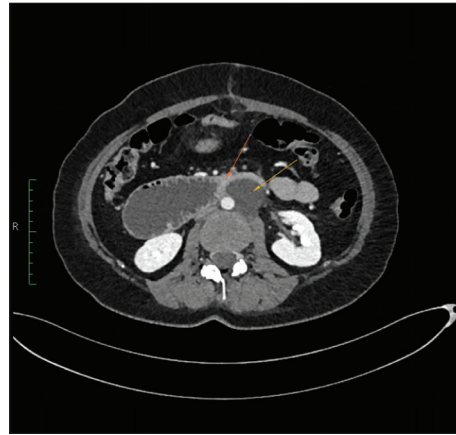
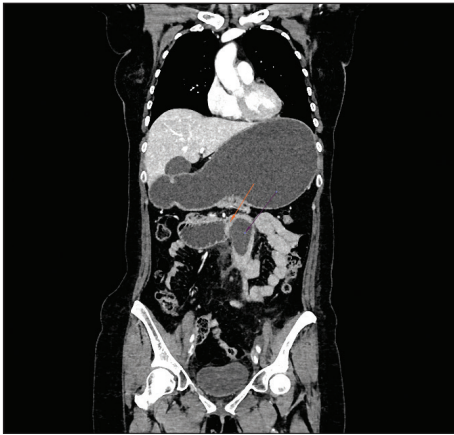


Fig. 11. High small intestinal obstruction due to the compression of the duodenum by a lymphocyst. Coronal section. An orange arrow — distended duodenum, a maroon arrow — lymphocyst

Fig. 12. High small intestinal obstruction due to the compression of the duodenum by a lymphocyst. Axial section. An orange arrow — distended duodenum, a yellow arrow — lymphocyst

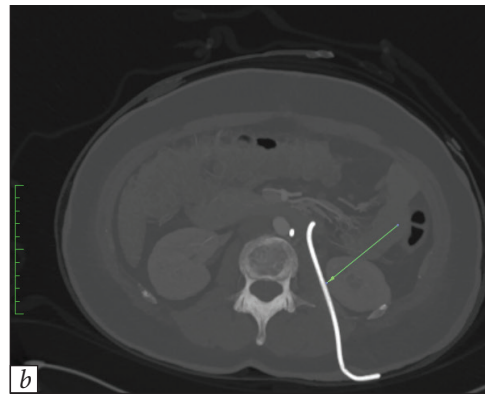
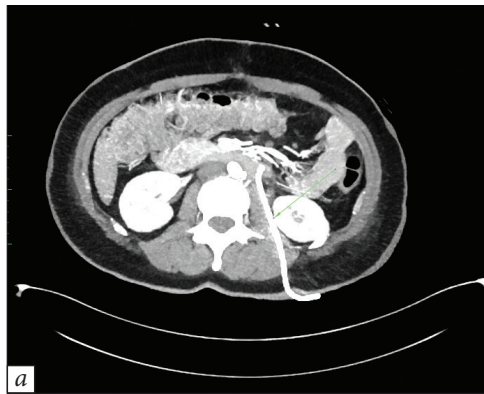


Fig. 13. Drainage of the retroperitoneal lymphocyst at the level of the left renal hilum under CT navigation, 17th day of the postoperative period. Axial sections: *a* — CT venous phase; *b* — CT venous phase (bone window translation)

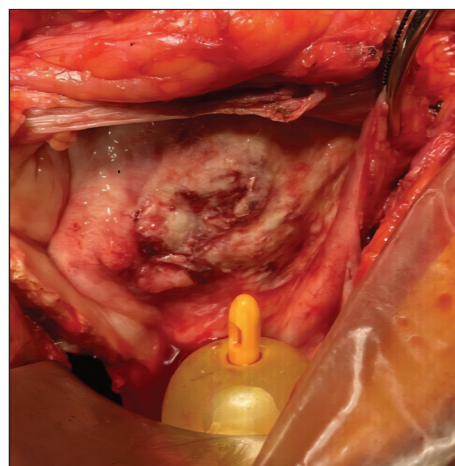


Fig. 14. Condition after drainage. Axial section. Yellow arrow — collapsed lymphocyst walls, orange arrow — intestinal wall, no intestinal obstruction

Fig. 15. Recurrent cervical cancer with bladder invasion. The tumor grows through the bladder wall to the mucous membrane



Fig. 16. Anterior pelvic exenteration in a patient with recurrent cervical cancer with bladder invasion. The stented ureters

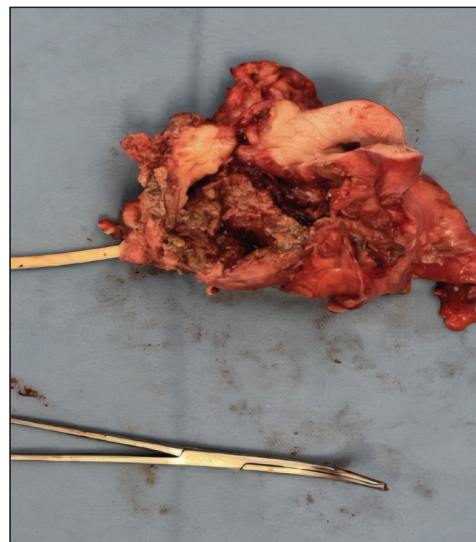


Fig. 17. The resected specimen (patient F.A.) after pelvic exenteration surgery

mous cell? Immunohistochemical study was recommended to exclude a neuroendocrine differentiation of the process. In the specimens of the right pelvic lymph nodes, carcinoma metastases are detected in one of the four examined lymph nodes. The same are in the specimens of the left para-aortic lymph nodes. In the specimen of the left pelvic and right para-aortic lymph nodes (4 + 4 pcs.) there are no signs of tumor growth.

The postoperative period was complicated by the formation of a symptomatic lymphocyst in the retroperitoneal paraaortic area (Fig. 11, 12). In December 2023, a drainage of the extraperitoneal lymphocyst at the level of the left kidney hilum was performed under CT navigation (Fig. 13, 14).

Immunohistochemical study confirmed endocervical adenocarcinoma, HPV-associated (Silva stromal invasion type C) (ICD-O code 8483/3). No expression of PD-L1 in the tumor was detected.

After discharge from the department, the patient received a course of chemoradiotherapy and bevacizumab.

A recurrence of the disease was diagnosed in October 2024, according to CT scan data, namely, multiple secondary bone lesions, mainly in the lower and cervical spine. The patient was treated by 3 courses of platinum-containing chemotherapy and zoledronic acid. She is currently receiving ibadronic acid in pills.

Case 3. Patient F.A., 34 years old, diagnosed with CC stage IIa, cT2aN0M0 G₁. Juvenile diabe-

tes mellitus type I, insulin-dependent, crisis course of the disease. In January 2019, the patient complained of the abnormal bleeding from the genital tract, a biopsy of the cervix was taken, and hemostatic therapy was performed. Pathohistological conclusion: squamous cell non-keratinizing carcinoma of the cervix G₁. In 2019, she received a course of combined radiation therapy against the background of competitive chemotherapy with bleomycin. In 2020, clinically and by CT data, an increase in the right inguinal lymph nodes, as well as pelvic and para-aortic ones, was noted, however, by the biopsy results, no tumor growth was detected morphologically. In July, 2022 complaints of gross hematuria with clots appeared. An endoscopic revision of the bladder was performed with evacuation of blood clots, and a biopsy was taken. Immunohistochemical study demonstrated the growth of squamous cell carcinoma of the cervix into the bladder wall.

In February 2023, surgical treatment was performed in the following scope: Anterior pelvic exenteration with ileocystoneoplasty, stenting of both ureters (Fig. 15, 16). Pathohistological conclusion: In the cervix, tumor growth is detected, the morphological structure of which corresponds to poorly differentiated G₃ squamous cell carcinoma. The tumor grows into the cervix, the wall of the bladder, and through the wall to the mucous membrane. Lymphovascular invasion is detected, and tumor thrombi are present in the vessels of the

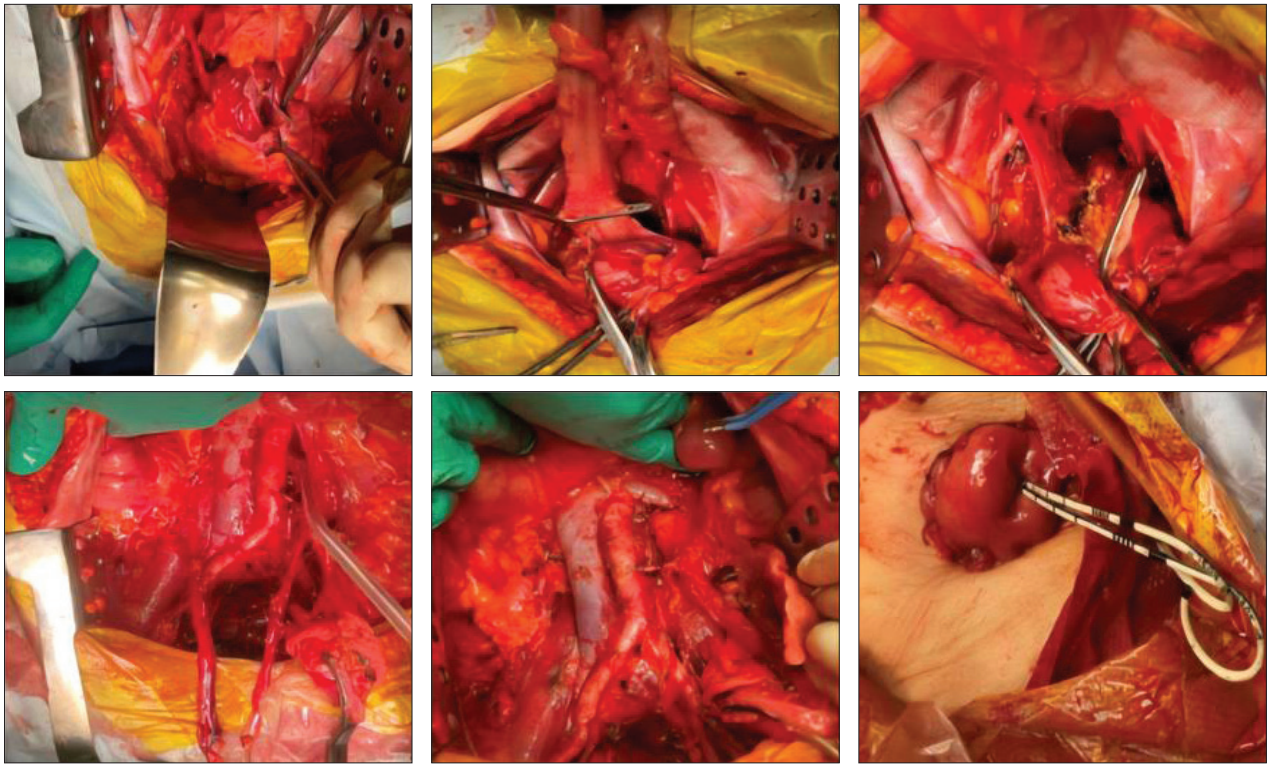


Fig. 18. Total pelvic exenteration, para-aortic lymphadenectomy. Colo-ureterostomy



Fig. 19. Total pelvic exenteration, para-aortic lymphadenectomy. Colo-ureterostomy. Perineal stage of the surgery

bladder wall. There is perineural invasion of the tumor in the cervix. Tumor elements are not identified in the marked resection margins. No tumor elements were detected in the lymph nodes rpT4pN0(0/4) LVI1 Pn1 R0 (03/09/2023).

From February to November 2023, she received 6 courses of chemotherapy using gemcitabine and 2 courses using vinorelbine. She was examined for the presence of PD-L1 protein in the tumor: expression was present. The patient died 11 months after surgery due to pneumonitis.

Case 4. Patient F.A., 32 years old, diagnosed with CC stage IIIc, cT3bN1M0 G₂. In October 2022, the patient noticed abnormal bloody discharge from the genital tract. Treatment began in March 2023 with uterine artery embolization. Pathohistological conclusion: moderately differentiated squamous cell carcinoma of the cervix. From April 2023 to August 2023, the patient received a course of chemoradiation therapy, namely a course of definitive radiotherapy to the pelvis in a total dose of 50.4 Gy/28 fractions + week radiosensitiza-

tion with Cisplatin in a dose of 40 mg/m² (5 injections) with a subsequent boost to the primary tumor, parametria, and previously enlarged lymph nodes in a total focal dose of 16 Gy/8 fractions. Brachytherapy was not performed due to the technical impossibility.

After massive bleeding from the cervix with hemorrhagic shock 17/01/2024, the surgery was performed: lower midline laparotomy, ligation of the internal iliac arteries, round and infundibulo-pelvic ligaments of the uterus. The patient received 5 courses of chemotherapy (paclitaxel + cisplatin). No expression of PD-L1 in the tumor was detected.

Diagnosis upon admission to the National Cancer Institute: CC stage IIIc1 cT3bN1M0 after chemoradiotherapy. Condition after 5 courses of chemotherapy and surgical treatment (20/08/2024). Ureterohydronephrosis right II—III degree. Post-radiation proctitis. Continuation of the disease. CT scan of the chest, abdominal cavity and pelvis, and MRI scan of the pelvis were performed. Diagnosis: CC T3bN1M0G₂, involving the right ureter. Local tissue defect on the right — uterine body, cervix, vagina, and right ureter, which is connected by a wide fistulous passage with local fluid sac in the right iliac region. A vesico-vaginal fistula has formed. Persistent stenosis of the right ureter in the pelvic part, defect of the juxta-vesical part. Right ureterohydronephrosis of the 2nd—3rd degree. Radiological signs of metastatic lesion: common iliac lymph node on the left and external iliac lymph node on the left.

The patient was urgently hospitalized to the National Cancer Institute with massive bleeding, hemostatic vaginal tamponade, and signs of hemorrhagic shock. On August 20, 2024, an urgent surgical intervention was performed in the following scope: Mid-lower-midline laparotomy, adhesiolysis. Anterior pelvic exenteration: bladder extirpation, hysterectomy with bilateral salpingo-oophorectomy, total vaginectomy, appendectomy, Bricker urinary diversion, abdominal debridement, and drainage. (Fig. 17). Pathohistological conclusion: Invasive squamous cell carcinoma G₃ with spread to the vagina, growth into the bladder mucosa and urethra, lymphovascular and perineural invasion, widespread necrosis of tumor tissue. In the examined areas of the submucosal adipose tissue of the rectum and the fascia of the pelvic wall, the growth of a similar tumor is determined.

The patient died in February 2025, 5 months after anterior pelvic exenteration surgery, from disease progression (the appearance of a recurrent tumor in the soft tissues of the right pelvic wall, soft tissues of the right abdominal wall according to MRI data of the pelvis and abdomen with the intravenous contrast enhancement).

Case 5. Patient P.O., 62 years old, diagnosed with CC stage IVa cT4aN0M0 G₂. The disease was manifested in January 2021 with stool disorders. The patient was examined by a proctologist. A colonoscopy was performed, and a biopsy of the cervix was taken. Histopathological conclusion: squamous cell carcinoma of the cervix with the growth into the intestinal wall. According to clinical and radiological findings, rectovaginal fistula was diagnosed. The patient received 3 courses of neoadjuvant chemotherapy with the paclitaxel + cisplatin regimen.

In June 2021, the patient was operated at the National Cancer Institute. The scope of the operation was: Total pelvic exenteration. Para-aortic lymphadenectomy. Monoureterosigmoidostomy formation. (Fig. 18, 19). Pathohistological conclusion: Squamous cell carcinoma of the cervix after treatment infiltrates the entire thickness of the organ, spreads to the uterus body, and grows into the intestinal wall to the mucous layer, a tumor with pronounced dystrophic changes, necrosis, focal lymphovascular invasion, and perineural invasion. In the ovaries serous cysts, manifestations of chronic salpingitis. Uterine leiomyoma. In the urinary bladder, deep in the muscle layer, there is a single focus of accumulation of dystrophically changed tumor cells in a state of necrosis. The tumor grows into the intestine, forming an uterointestinal fistula. In all groups of examined lymph nodes: right pelvic (5 pieces), left pelvic (6 pieces), para-aortic (5 pieces), carcinoma metastases are not detected (April, 2021). The patient was observed without any signs of disease recurrence for 4 years after surgery.

Discussion

According to ESGO/ESTRO/ESP standards, the main method of treatment of patients with advanced stages of CC is chemoradiotherapy [4]. Moreover, even in the treatment of locally advanced CC, recent studies have not shown an ad-

vantage in the overall survival for patients treated with surgery after neoadjuvant chemotherapy compared to chemoradiation therapy [5, 6]. However, the presence of the residual disease after chemoradiation treatment is directly associated with the risk of relapse and poor survival [7]. According to a study by Platt et al. [7], surgery may be beneficial for patients with incomplete chemoradiation therapy, for certain histological subtypes of CC, or for a bulky residual disease. Moreover, the authors noted that the method of surgical intervention is a debatable issue, considering the possibility of both open and laparoscopic surgery, but are cautious about radical interventions due to an increased risk of the postoperative complications. Yang et al. [8] conducted a study on the survival of patients who underwent definitive hysterectomy after chemoradiation treatment for locally advanced adenocarcinoma of the cervix and concluded that patients under 60 years of age, with a tumor above 4 cm, stage IIB, and persistent residual disease after chemoradiotherapy would most likely benefit from hysterectomy. Moreover, hysterectomy was associated with a lower rate of locoregional recurrence; however these findings did not reach statistical significance.

There is an extensive discussion about the feasibility of performing systemic lymphadenectomy for advanced CC. It is known that the probability of the metastatic involvement of the para-aortic lymph nodes increases with the disease stage, reaching 21%–37% in stage III [9]. The NCCN guidelines recommend the surgical staging of the para-aortic lymph nodes before chemoradiotherapy to determine accurately the lymph node involvement. However, surgery for this purpose is associated with risks such as lymph cysts, possible delays in radiation therapy, and increased length of hospital stay [10]. Jiang et al. [9] compared the main complications that occur during the treatment of advanced CC in a group of patients who underwent surgical staging (i.e., para-aortic lymphadenectomy) and those who did not. The incidence of grade 3–4 myelosuppression, grade 3–4 acute gastrointestinal disorders, and lower extremity edema did not differ significantly between the groups. The authors concluded that the detection of the metastatic para-aortic lymph node is important for tailoring chemoradiotherapy plans for each patient [9]. Gold et al. [11], who

analyzed data from the GOG 85, GOG 120, and GOG 165 studies, found that surgical staging improves disease-free survival (50% vs. 36%) and overall survival (54% vs. 40%), especially for stage III/IV compared to stage II.

In our patient S.E. (case 2), the pelvic and para-aortic lymphadenectomy was performed and, by histopathological examination, most of lymph nodes were metastatically affected; the patient is still alive. Our data are consistent with those by Marnitz et al. [12], who found that the removal of tumor-affected lymph nodes improves survival. A retrospective analysis by Cosin et al. [13], who demonstrated that removal of macroscopically altered metastatic lymph nodes significantly improves clinical outcomes, can be interpreted in a similar way.

Jiang et al. [9] reported the lymphocyst incidence of 9.3% and one case of intestinal obstruction, thus concluding that systemic lymphadenectomy is safe and clinically useful in patients with advanced CC [9]. It should be noted that in the study, para-aortic lymphadenectomy was performed laparoscopically, which was explained by the aim to reduce the risks of postoperative complications.

Most researchers consider that pelvic exenteration in the treatment of locally advanced CC is effective, despite its technical complexity, high level of intra- and postoperative complications, high postoperative mortality, and problems with subsequent rehabilitation of patients [14, 15]. According to a study by Bouraoui and Bouaziz [15], the a negative resection margin after pelvic exenteration was an important prognostic factor affecting overall and recurrence-free survival. Graves et al. [16] noted that pelvic exenteration can be a curative operation in more than half of patients with locally advanced CC, provided that there is no lymph node involvement, and also conclude that the cleanliness of tumor resection margins is important for overall survival after this operation. All these literature data are consistent with the results of the treatment of patient P.O. (case 5), where negative tumor resection margins and the absence of metastases in all groups of removed lymph nodes were obtained — the patient is alive and has no signs of recurrence to date.

Summarizing the above, it should be noted that the surgical method in selected cases of advanced CC may be an option that will ensure survival,

the possibility of continuing cancer treatment, and sometimes even a radical cure for patients. In most cases, treatment of the advanced CC and their recurrences is carried out using radiation and chemotherapy, or palliative and symptomatic treatment. The use of immunotherapy in patients with recurrent and advanced CC is promising today, especially if the tumors express PD-L1

and possess microsatellite instability. The surgical method can be leading and effective in some cases if the operation is performed on a radical scale. Important in this regard are the clinical experience, high level of surgical skills, the presence of a multidisciplinary team, and the technical equipment of the medical center for performing such operations.

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НЕСТАНДАРТНІ СТРАТЕГІЇ В ЛІКУВАННІ ПОШИРЕНОГО РАКУ ШИЙКИ МАТКИ (СЕРІЯ ВИПАДКІВ)

Стан питання. Рак шийки матки продовжує бути провідним онкологічним захворюванням, що уражує жінок як молодого, так і похилого віку. На поширених стадіях раку шийки матки вибір лікувальної тактики вирішується на користь хіміопроменевої терапії. Однак у низці випадків хірургічне лікування в радикальному об'ємі може бути єдиним ефективним заходом. **Матеріали та методи.** Представлено 5 нестандартних випадків хірургічного лікування пацієнок, хворих на розповсюджений рак шийки матки (стадії IIa — IVa), які були прооперовані на базі науково-клінічного відділу новоутворень жіночої репродуктивної системи Національного інституту раку з 2021 по 2025 роки. **Результати.** В усіх представлених клінічних випадках розповсюдженого раку шийки матки хворим було виконано хірургічне лікування в радикальному обсязі, що мало беззаперечний куративний ефект в усіх пацієнок на час його виконання. У подальшому спостереженні дві пацієнтки живі без будь-яких проявів захворювання; дві померли від прогресування захворювання і одна пацієнтка жива, однак отримує лікування з приводу рецидиву хвороби у кістки. **Висновки.** Попри те, що у більшості випадків лікування поширених стадій раку шийки матки є хімотерапевтичним, хірургічний метод в окремих випадках може бути провідним та ефективним, якщо операція виконується в радикальному обсязі. Важливе значення при цьому мають клінічний досвід, високий рівень хірургічних навичок, наявність мультидисциплінарної команди та технічного оснащення медичного центру для проведення таких операцій.

Ключові слова: поширений рак шийки матки, радикальне хірургічне лікування, симптомна лімфоденектомія заочеревинної ділянки, екзентерація тазу.