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research article

Cervix-Online computer program: 27 years of hospital-based clinical registry for cervical cancer at the University Medical Centre Maribor

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Background. Clinical registries are designed to collect quality data about the care for cancer patients in order to improve it. They gather data that are generated during diagnosis and cancer treatment and also post-treatment follow-up. Analysis of collected data allows an improvement in the quality of patient care and a comparison with other health care providers. The aim of the present article is to describe the current version and practice of hospital-based cervical cancer registry in UKC Maribor.

Materials and methods. The first questionnaire for monitoring patients with cervical cancer was introduced at the Department of Gynecologic and Breast Oncology of the Maribor General Hospital in 1994. Since then, the principles for treating cervical cancer have been revised on several occasions. Therefore, based on our experience and new approaches to treatment, we have frequently amended the questionnaire content. It was redesigned into a form that is currently in use and transformed into a Cervix-Online computer program in 2014.

Results. Over the last 27 years, we have collected data on cervical cancer patients treated at the University Medical Centre Maribor and former Maribor General Hospital. The Cervix-Online computer program that was developed for this purpose enabled a rapid and reliable collection, processing and analysis of 116 different data of patients with cervical cancer, including general data, history, diagnostic procedures, histopathological examination results, treatment methods, and post-treatment follow-ups.

Conclusions. The hospital-based cervical cancer registry with Cervix-Online computer program enables the collection of data to enhance diagnosis and the treatment of cervical cancer patients, the organization of day-to-day service, as well as the comparison of our treatment results with national and international standards. Incomplete or incorrect data entry, however, might pose a limitation of the clinical registry, which depends on several healthcare professionals involved in the diagnostic procedures, treatment, and follow-up of cervical cancer patients.

Key words: hospital-based clinical registry; computer program; cervical cancer

Introduction

Cancer registries are established with the goal of systematic collection, storage, analysis, interpretation and reporting of data on subjects with cancer. There are two main types of cancer registries: hospital-based and population-based cancer registry. The former is dealing with recording of information on cancer patients treated in particular hospital, while the latter collects data on all new cancer patients in a well-defined population with the intention of describing the extent and nature of

cancer burden in this particular community and assist in the establishment of public health priorities. Their data provide a source for etiological studies and may help in assessing the effectiveness of cancer control activities.[1]

One of the oldest population-based cancer registries in Europe was established in Slovenia. It is called the Cancer Registry of the Republic of Slovenia and was founded at the Institute of Oncology Ljubljana in 1950. This registry is monitoring the population burden for all malignant and pre-malignant oncological diseases in Slovenia.[2] The forth extensive report on the survival of Slovenian cancer patients diagnosed between 1997 and 2016 was presented recently showing increasing survival of cancer patients over the last 20 years.[3] In order to improve the survival rate, earlier stages of the disease should be detected and modern treatments widely available. The challenge in the future is to establish monitoring of quality of care by establishing clinical registries for the five most common cancers.[4]

The national screening programme for early detection of cervical cancer ZORA, introduced in 2003, resulted in the yearly incidence decrease by 3.5% in the last ten years.[4] On the other hand the population–based registry report shows no increase in the survival rate from this disease when comparing women diagnosed between 1997–2001 and 2012–2016.[3] The Cancer Registry of RS as well as Cervical Cancer Screening registry ZORA within the ZORA program also produce yearly reports to screening providers and annual reports where some of the indicators are related to quality of care and also treatment. However, it is true, that additional data can provide more guidance to improve the quality of care. Acquiring of this kind of data requires establishing of a clinical registry where a significantly more extensive set of clinical data are collected. This would be easier to do if the Slovenian health care system was based on a single information platform.[3] The first special clinical registry in Slovenia was the Clinical Registry of Skin Melanoma founded in 2017.

Following the aims of the National Cancer Control Plan 2017–2021, the Institute of Oncology Ljubljana is establishing a system for collecting and reporting the extended information for patients diagnosed with the most common cancers: breast, prostate, colon and rectum, lung and skin melanoma.[2]

Department of Gynaecologic and Breast Oncology of University Medical Centre Maribor has a long tradition of collecting clinical data on gynaecological cancers. In 1994 we introduced seven different hospital-based clinical registries for gynaecological (vulvar, vaginal, cervical, endometrial, ovarian, fallopian tube cancer) and breast cancer. A computer program has been designed for all of them and articles on the use of this software to follow-up patients with ovarian malignancies were published in 1996 and 1999 and for breast cancer patients in 2019.[6-8]

Registry for cervical cancer records data known to be associated with high risk for cervical cancer, such as high parity, specifically seven prior full-term pregnancies, early age at first intercourse, before 20 years of age, cigarette smoking, both active and passive and the use of combined oral contraceptives.[9-13] Lower socio-economic status with

UKC MARIBOR

Division of Gynecology and Perinatology

CERVIX

G1 Year/No.:

G2 NAME

G3 AGE G4 PERS. NO. G5 INSURANCE

G6 DATE OF RECENT EXAMINATION (or EX):

G7 CONDITION AT LAST CHECK-UP (or EX):

0 alive, no symptoms
1 alive, partial remission
2 alive, stable disease
3 alive, relapse
4 alive, progressive disease
5 alive, condition unknown
6 ex due to cervix malignancy
7 ex during treatment
8 ex due to other disease, no cervical cancer
9 ex due to other disease, cervical cancer present
10 ex, cause unknown
11 condition unknown

G8 DG: G9 Date of DG:

G10 STAGE: 1 IA1 2 IA2 3 IB1 4 IB2 5 IIA1 6 IIA2 7 IIB 8 IIIA 9 IIIB 10 IVA 11 IVB

G11 DIFFERENTIATION: 1 G1 2 G2 3 G3

G12 TREATMENT:

0 no treatment
1 cone biopsy
2 hysterectomy
3 WMN
4 non-radical surgery
5 neoadjuvant CT
6 full CT
7 non-complete CT
8 second line CT
9 tele-RT
10 brachy-RT
11 other (details):

G13 No. OF SURGERIES:

G14 PRIMARY TREATMENT RESULTS:

0 complete remission
1 partial remission
2 unaltered state
3 progression
4 exitus
5 other (details):

G15 FIRST RELAPSE

0 no
1 yes, cervix
2 yes, vagina
3 yes, pelvis
4 yes, abdomen
5 yes, periaortic nodes
6 remote
7 unknown

G16 FIRST RELAPSE DATE

G17 FIRST RELAPSE TREATMENT

0 no
1 surgical
2 CT
3 RT
4 other (details)

G18 SECOND RELAPSE

0 no
1 yes, cervix
2 yes, vagina
3 yes, pelvis
4 yes, abdomen
5 yes, periaortic nodes
6 remote
7 remote

G19 SECOND RELAPSE DATE

G20 SECOND RELAPSE TREATMENT

0 no
1 surgical
2 CT
3 RT
4 other (details)

PC No.:

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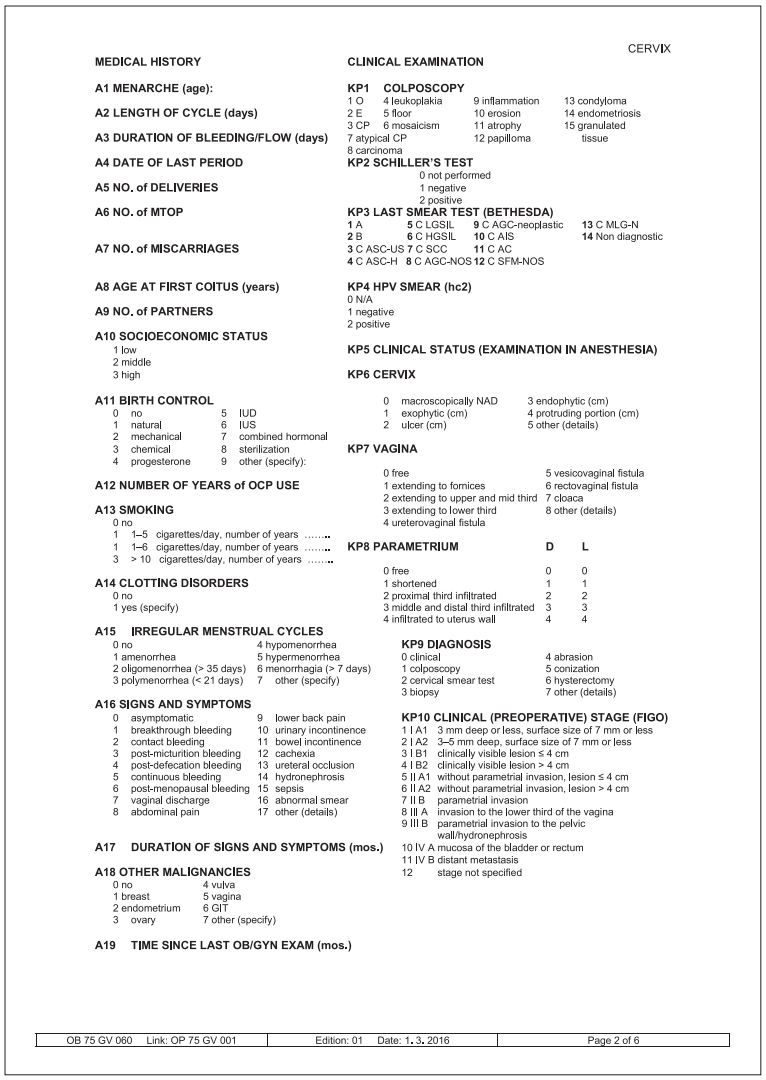
FIGURE 1. General data.

CT = chemotherapy; RT = radiotherapy



CERVIX

MEDICAL HISTORY

A1 MENARCHE (age):

A2 LENGTH OF CYCLE (days)

A3 DURATION OF BLEEDING/FLOW (days)

A4 DATE OF LAST PERIOD

A5 NO. of DELIVERIES

A6 NO. of MTOP

A7 NO. of MISCARRIAGES

A8 AGE AT FIRST COITUS (years)

A9 NO. of PARTNERS

A10 SOCIOECONOMIC STATUS
1 low
2 middle
3 high

A11 BIRTH CONTROL

0	no	5	IUD
1	natural	6	IUS
2	mechanical	7	combined hormonal
3	chemical	8	sterilization
4	progesterone	9	other (specify):

A12 NUMBER OF YEARS of OCP USE

A13 SMOKING
0 no
1 1–5 cigarettes/day, number of years .....
1 1–6 cigarettes/day, number of years .....
3 > 10 cigarettes/day, number of years .....

A14 CLOTTING DISORDERS
0 no
1 yes (specify)

A15 IRREGULAR MENSTRUAL CYCLES

0	no	4	hypomenorrhea
1	amenorrhea	5	hypermenorrhea
2	oligomenorrhea (> 35 days)	6	menorrhagia (> 7 days)
3	polymenorrhea (< 21 days)	7	other (specify)

A16 SIGNS AND SYMPTOMS

0	asymptomatic	9	lower back pain
1	breakthrough bleeding	10	urinary incontinence
2	contact bleeding	11	bowel incontinence
3	post-micturition bleeding	12	cachexia
4	post-defecation bleeding	13	ureteral occlusion
5	continuous bleeding	14	hydronephrosis
6	post-menopausal bleeding	15	sepsis
7	vaginal discharge	16	abnormal smear
8	abdominal pain	17	other (details)

A17 DURATION OF SIGNS AND SYMPTOMS (mos.)

A18 OTHER MALIGNANCIES

0	no	4	vulva
1	breast	5	vagina
2	endometrium	6	GIT
3	ovary	7	other (specify)

A19 TIME SINCE LAST OB/GYN EXAM (mos.)

CLINICAL EXAMINATION

KP1 COLPOSCOPY

1 O	4 leukoplakia	9 inflammation	13 condyloma
2 E	5 floor	10 erosion	14 endometriosis
3 CP	6 mosaicism	11 atrophy	15 granulated tissue
7 atypical CP		12 papilloma	
8 carcinoma			

KP2 SCHILLER'S TEST
0 not performed
1 negative
2 positive

KP3 LAST SMEAR TEST (BETHESDA)

1 A	**5** C LGSIL	**9** C AGC-neoplastic	**13** C MLG-N
2 B	**6** C HGSIL	**10** C AIS	**14** Non diagnostic
3 C ASC-US	**7** C SCC	**11** C AC	
4 C ASC-H	**8** C AGC-NOS	**12** C SFM-NOS	

KP4 HPV SMEAR (hc2)
0 N/A
1 negative
2 positive

KP5 CLINICAL STATUS (EXAMINATION IN ANESTHESIA)

KP6 CERVIX

0	macroscopically NAD	3	endophytic (cm)
1	exophytic (cm)	4	protruding portion (cm)
2	ulcer (cm)	5	other (details)

KP7 VAGINA

0	free	5	vesicovaginal fistula
1	extending to fornices	6	rectovaginal fistula
2	extending to upper and mid third	7	cloaca
3	extending to lower third	8	other (details)
4	ureterovaginal fistula		

KP8 PARAMETRIUM

	D	L
0 free	0	0
1 shortened	1	1
2 proximal third infiltrated	2	2
3 middle and distal third infiltrated	3	3
4 infiltrated to uterus wall	4	4

KP9 DIAGNOSIS

0	clinical	4	abrasion
1	colposcopy	5	conization
2	cervical smear test	6	hysterectomy
3	biopsy	7	other (details)

KP10 CLINICAL (PREOPERATIVE) STAGE (FIGO)

1 I A1	3 mm deep or less, surface size of 7 mm or less
2 I A2	3–5 mm deep, surface size of 7 mm or less
3 I B1	clinically visible lesion ≤ 4 cm
4 I B2	clinically visible lesion > 4 cm
5 II A1	without parametrial invasion, lesion ≤ 4 cm
6 II A2	without parametrial invasion, lesion > 4 cm
7 II B	parametrial invasion
8 III A	invasion to the lower third of the vagina
9 III B	parametrial invasion to the pelvic wall/hydronephrosis
10 IV A	mucosa of the bladder or rectum
11 IV B	distant metastasis
12	stage not specified

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FIGURE 2. Medical history, clinical examination, clinical stage (preoperative International Federation of Gynecology and Obstetrics [FIGO] stage).

AGC - neoplastic = atypical glandular cells - neoplastic; AGC-NOS = atypical glandular cells - not otherwise specified; AIS = adenocarcinoma in situ; AC = adenocarcinoma; ASC-US = atypical squamous cells - of undetermined significance; ASC-H = atypical squamous cells - cannot exclude HSIL; GIT = gastrointestinal tract; HGSIL = high grade squamous intraepithelial lesion; IUD = intrauterine device; IUS = intrauterine system; LGSIL = low grade squamous intraepithelial lesion; MLG-N = other malignant cells - inevaluable; MTOP = medical termination of pregnancy; N/A = not available; SCC = squamous cell carcinoma; SFM-NOS = suspicious for malignancy - not otherwise specified

lower educational attainment, obesity and neighbourhood poverty are related to lower rates of cervical cancer screening and therefore later cancer detection.[14-16] Human papillomavirus (HPV) can be detected in more than 99% of cervical cancers and is essential for the malignant transformation. HPV types are classified as carcinogenic (class I) or high-risk HPV (hr HPV) types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59).[17] The combined prevalence of HPV 16/18 among HPV-positive cervical cancers in central and eastern European countries is 87.5%.[18]

Cervical cancer is the third most common cancer and the fourth leading cause of cancer death in women worldwide.[11] According to the International Agency for Research on Cancer (IARC) estimates of the cancer burden in Europe, approximately 33.000 women were diagnosed with cervical cancer and 15.000 died from the disease in 2018.[19]

We believe that this comprehensive hospital-based clinical registry could play a vital role in monitoring and improving the quality of care of cervical cancer patients as well as research in the field of cervical cancer diagnosis and treatment. The registry might become even more important due to the global WHO cervical cancer elimination goal.

The aim of this manuscript is to present our registry called Cervix-Online. It is well structured and datasets are reasonable. We believe that it could be of interest to other hospital-based cervical cancer registries (nationally as well as internationally) as well as for national cancer and national screening registries.

Materials and methods

Over the past decades, the treatment of cervical cancer has changed dramatically in terms of surgery, radiotherapy, and systemic treatment. Regarding our previous experience with collecting cancer patient's data including all relevant data, the context of the inquiry for cervical cancer has been modified and redesigned for current use. The updated inquiry protocol served as a model for developing an adequate computer program called Cervix-Online in 2014 with the purpose to record data during diagnostics, treatment and follow-up of patients.

After the patients complete their primary treatment, data are recorded using the Cervix-Online computer program. Paper forms are used first, during patient's interview with the attending physician, and the data are later transferred to the Cervix-Online computer program. The form is available and filled with new information upon any following visit. The front page of Cervix-Online contains basic information regarding stage of the disease, initial treatment and its results, relapses and their treatment. It is followed by patient's history, signs and symptoms and the findings of colposcopy, cytology and clinical examination together with different tests used to determine the stage of the disease. In the following three figures details about surgery, radiotherapy, chemotherapy and hormone therapy are included together with detailed pathologic and histologic report.

Results

The inquiry for cervical cancer covers 116 different items divided into following sections: general data, medical history, clinical examination, tests and examinations, treatment, histopathology, systemic treatment, and follow-up.

General data are partly collected with the establishment of cervical cancer diagnosis consisting of identification and treatment data at the end of primary treatment (Figure 1).

Nineteen anamnestic data sets focus on known risk factors for cervical cancer, current symptoms, and signs. Among the risk factors, detailed data on menstrual history, sexual and reproductive data, birth control, smoking, and clotting disorders are recorded. Detailed data are listed in Figure 2. The anamnestic data include signs and symptoms, the duration of symptoms is recorded, as well as the presence of other malignancies and the time since last gynaecological examination.

Next section covers clinical examination with 10 parameters, including colposcopy, Schiller's (iodine) test, the results of last Pap smear test according to Bethesda System, results of high-risk HPV test, and clinical status during examination under general anaesthesia as well as the clinical appearance of cervix, vagina and parametria. Eventually, the preoperative International Federation of Gynecology and Obstetrics (FIGO) stage is determined (Figure 2).

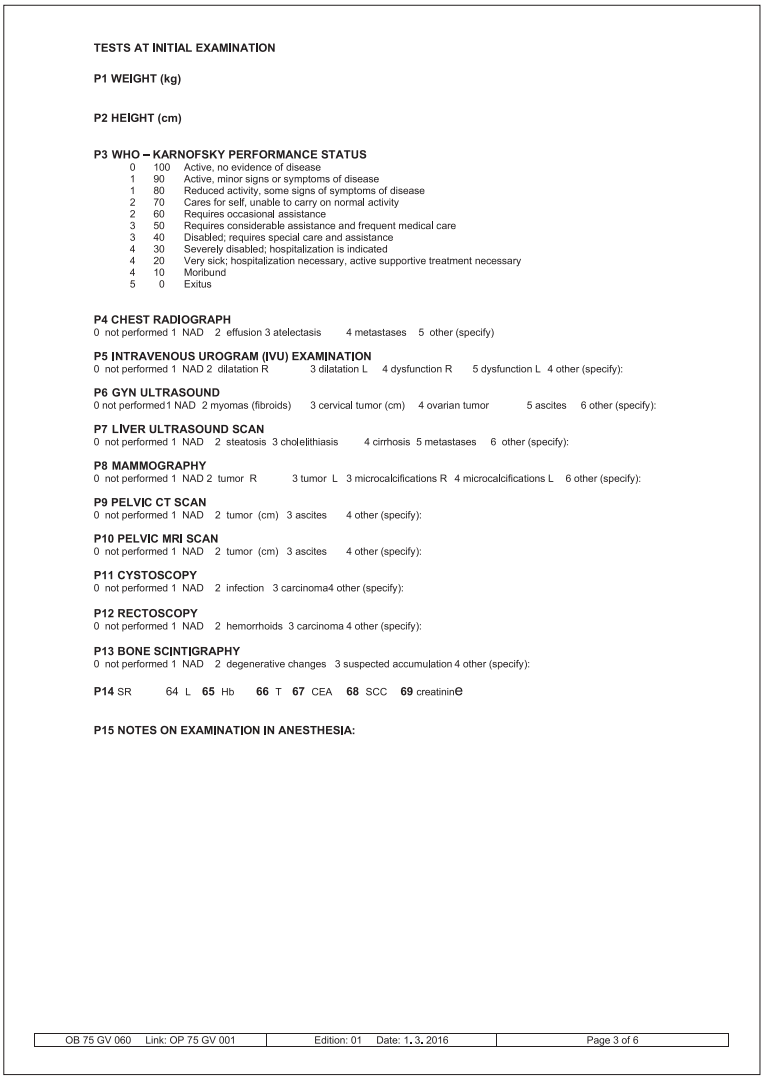
The following inquiry section contains data about initial examination, different tests and investigations prior to treatment. At the end of this section, a gynaecological examination report under anaesthesia is recorded (Figure 3).

The section containing data about the surgical procedure and postoperative care includes 13 parameters. Due to a high bladder dysfunction incidence following radical surgery special attention is given to bladder drainage, removal of drains and spontaneous micturition after surgery (Figure 4). For easier and faster completion of the inquiry, types of surgical procedures are listed as well as the most common complications during surgery and postoperative complications.

For radiation therapy, six boxes were designed. At our institution, radiotherapy is performed at the Department of Oncology; data about this treatment are completed after the treatment has been concluded, at the first follow-up visit at the latest.

In the chemotherapy section, details about the used agents are listed together with doses and complications. At the end, the chemotherapy results are recorded. Type, dosage, duration and results of hormonal therapy are also included.

In the next section, data about histopathologic examination of tumour, lymph nodes and other tissues removed during surgery are collected. The first part of this section includes data about cervical cone biopsy. Tumour differentiation, depth of invasion, size of tumour, lymphovascular invasion and lymph node status are recorded (Figure 5). At the end of this section, a FIGO stage after definitive histology is determined. Full data on histopathology are usually available after the patient was discharged; consequently, this part of the inquiry is completed later on.



TESTS AT INITIAL EXAMINATION

P1 WEIGHT (kg)

P2 HEIGHT (cm)

P3 WHO – KARNOFSKY PERFORMANCE STATUS

0	100	Active, no evidence of disease
1	90	Active, minor signs or symptoms of disease
1	80	Reduced activity, some signs of symptoms of disease
2	70	Cares for self, unable to carry on normal activity
2	60	Requires occasional assistance
3	50	Requires considerable assistance and frequent medical care
3	40	Disabled; requires special care and assistance
4	30	Severely disabled; hospitalization is indicated
4	20	Very sick; hospitalization necessary, active supportive treatment necessary
4	10	Moribund
5	0	Exitus

P4 CHEST RADIOGRAPH
0 not performed 1 NAD 2 effusion 3 atelectasis 4 metastases 5 other (specify)

P5 INTRAVENOUS UROGRAM (IVU) EXAMINATION
0 not performed 1 NAD 2 dilatation R 3 dilatation L 4 dysfunction R 5 dysfunction L 4 other (specify):

P6 GYN ULTRASOUND
0 not performed 1 NAD 2 myomas (fibroids) 3 cervical tumor (cm) 4 ovarian tumor 5 ascites 6 other (specify):

P7 LIVER ULTRASOUND SCAN
0 not performed 1 NAD 2 steatosis 3 cholelithiasis 4 cirrhosis 5 metastases 6 other (specify):

P8 MAMMOGRAPHY
0 not performed 1 NAD 2 tumor R 3 tumor L 3 microcalcifications R 4 microcalcifications L 6 other (specify):

P9 PELVIC CT SCAN
0 not performed 1 NAD 2 tumor (cm) 3 ascites 4 other (specify):

P10 PELVIC MRI SCAN
0 not performed 1 NAD 2 tumor (cm) 3 ascites 4 other (specify):

P11 CYSTOSCOPY
0 not performed 1 NAD 2 infection 3 carcinoma4 other (specify):

P12 RECTOSCOPY
0 not performed 1 NAD 2 hemorrhoids 3 carcinoma 4 other (specify):

P13 BONE SCINTIGRAPHY
0 not performed 1 NAD 2 degenerative changes 3 suspected accumulation 4 other (specify):

P14 SR 64 L **65** Hb **66** T **67** CEA **68** SCC **69** creatinine

P15 NOTES ON EXAMINATION IN ANESTHESIA:

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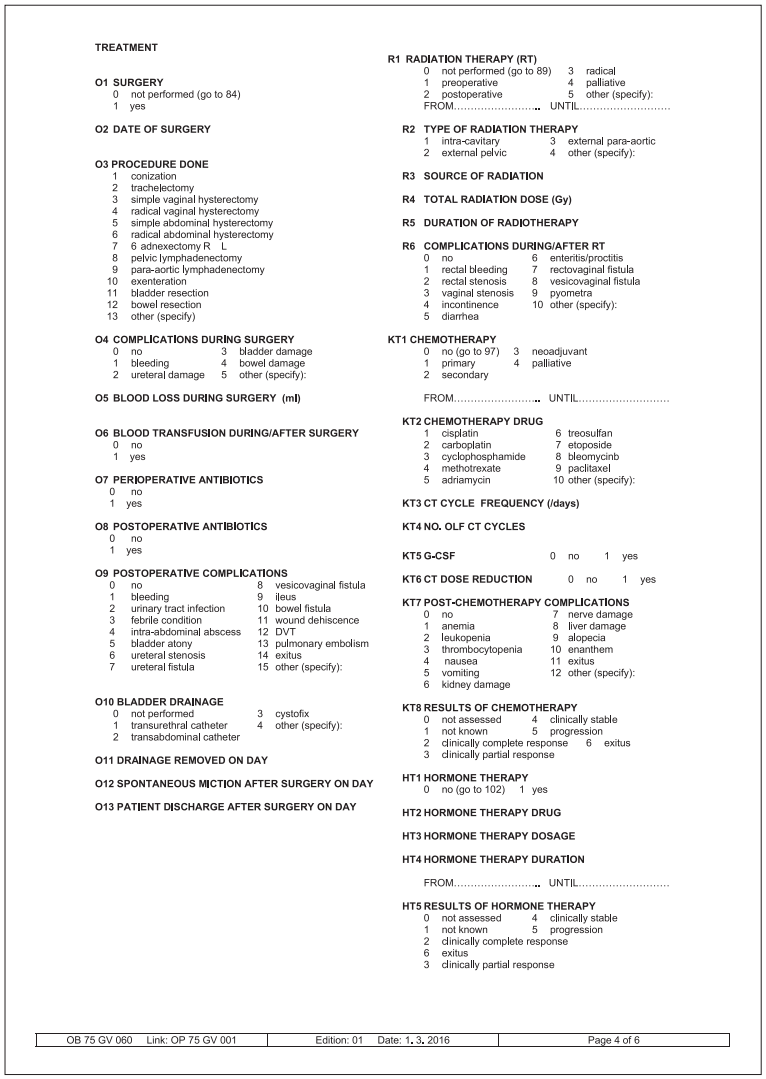
FIGURE 3. Tests at initial examination.

CEA = carcinoembryonic antigen; L = left; NAD = no evidence of disease; R = right; SCC = squamous cell carcinoma antigen



TREATMENT

O1 SURGERY
0 not performed (go to 84)
1 yes

O2 DATE OF SURGERY

O3 PROCEDURE DONE
1 conization
2 trachelectomy
3 simple vaginal hysterectomy
4 radical vaginal hysterectomy
5 simple abdominal hysterectomy
6 radical abdominal hysterectomy
7 6 adnexectomy R L
8 pelvic lymphadenectomy
9 para-aortic lymphadenectomy
10 exenteration
11 bladder resection
12 bowel resection
13 other (specify)

O4 COMPLICATIONS DURING SURGERY
0 no 3 bladder damage
1 bleeding 4 bowel damage
2 ureteral damage 5 other (specify):

O5 BLOOD LOSS DURING SURGERY (ml)

O6 BLOOD TRANSFUSION DURING/AFTER SURGERY
0 no
1 yes

O7 PERIOPERATIVE ANTIBIOTICS
0 no
1 yes

O8 POSTOPERATIVE ANTIBIOTICS
0 no
1 yes

O9 POSTOPERATIVE COMPLICATIONS
0 no 8 vesicovaginal fistula
1 bleeding 9 ileus
2 urinary tract infection 10 bowel fistula
3 febrile condition 11 wound dehiscence
4 intra-abdominal abscess 12 DVT
5 bladder atony 13 pulmonary embolism
6 ureteral stenosis 14 exitus
7 ureteral fistula 15 other (specify):

O10 BLADDER DRAINAGE
0 not performed 3 cystofix
1 transurethral catheter 4 other (specify):
2 transabdominal catheter

O11 DRAINAGE REMOVED ON DAY

O12 SPONTANEOUS MICTION AFTER SURGERY ON DAY

O13 PATIENT DISCHARGE AFTER SURGERY ON DAY

R1 RADIATION THERAPY (RT)
0 not performed (go to 89) 3 radical
1 preoperative 4 palliative
2 postoperative 5 other (specify):
FROM..... UNTIL.....

R2 TYPE OF RADIATION THERAPY
1 intra-cavitary 3 external para-aortic
2 external pelvic 4 other (specify):

R3 SOURCE OF RADIATION

R4 TOTAL RADIATION DOSE (Gy)

R5 DURATION OF RADIOTHERAPY

R6 COMPLICATIONS DURING/AFTER RT
0 no 6 enteritis/proctitis
1 rectal bleeding 7 rectovaginal fistula
2 rectal stenosis 8 vesicovaginal fistula
3 vaginal stenosis 9 pyometra
4 incontinence 10 other (specify):
5 diarrhea

KT1 CHEMOTHERAPY
0 no (go to 97) 3 neoadjuvant
1 primary 4 palliative
2 secondary
FROM..... UNTIL.....

KT2 CHEMOTHERAPY DRUG
1 cisplatin 6 treosulfan
2 carboplatin 7 etoposide
3 cyclophosphamide 8 bleomycinb
4 methotrexate 9 paclitaxel
5 adriamycin 10 other (specify):

KT3 CT CYCLE FREQUENCY (/days)

KT4 NO. OLF CT CYCLES

KT5 G-CSF 0 no 1 yes

KT6 CT DOSE REDUCTION 0 no 1 yes

KT7 POST-CHEMOTHERAPY COMPLICATIONS
0 no 7 nerve damage
1 anemia 8 liver damage
2 leukopenia 9 alopecia
3 thrombocytopenia 10 enanthem
4 nausea 11 exitus
5 vomiting 12 other (specify):
6 kidney damage

KT8 RESULTS OF CHEMOTHERAPY
0 not assessed 4 clinically stable
1 not known 5 progression
2 clinically complete response 6 exitus
3 clinically partial response

HT1 HORMONE THERAPY
0 no (go to 102) 1 yes

HT2 HORMONE THERAPY DRUG

HT3 HORMONE THERAPY DOSAGE

HT4 HORMONE THERAPY DURATION
FROM..... UNTIL.....

HT5 RESULTS OF HORMONE THERAPY
0 not assessed 4 clinically stable
1 not known 5 progression
2 clinically complete response
6 exitus
3 clinically partial response

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FIGURE 4. Treatment.

CT = chemotherapy: DVT = deep vein thrombosis; G-CSF = granulocyte colony stimulating factor

Detailed information about adjuvant or neoadjuvant chemotherapy is collected on a separate inquiry page (Figure 6).

The last section of the inquiry is designed for the follow-up (Figure 7). All 12 boxes are to be completed at every follow-up visit. Data collected at follow-ups are limited to the wellbeing of the patient, pain, discharge, bleeding, micturition, defecation and bowel movement, body weight, clinical examination, cervical smear, laboratory tests and the condition assessment of the patient.

All data collected with the paper inquiry are recorded with the Cervix-Online computer program used for processing data and statistical analysis.

Discussion

Slovenia is one of the European countries with the highest historical incidence of cervical cancer and one of the countries with the highest decrease of cervical cancer incidence over time.[20] The crude incidence of cervical cancer in Slovenia in the period 2013–2017 was 10.9/100.000 and the age standardized incidence was 7.0/100.000 with approximately 113 new cases yearly. In the same period, the crude death rate was 4.3/100.000 and age standardized death rate was 2.1/100.000 with the prevalence of 3490 women with cervical cancer on December 31, 2017.[21]

Only disease specific registries allow for comparisons of different treatments or therapeutic strategies. For that reason there is the need for the extended information on the quality of the primary treatment, adjuvant treatment, complications and time frame of work-up that influence final outcome of patients with cervical cancer. This is the kind of information that is usually not gathered in population–based registries. The need for clinical registries is evident.

The cervical cancer inquiry we present collects extended information; a total of 116 questions about cervical cancer patient medical history, clinical status, histopathological results, treatment and its outcome. It provides a base for improvements in monitoring the quality of care of cervical cancer patients, and research in the field of cervical cancer diagnosis and treatment. Some of the elements collected are essential for clinical management and others are not regularly used in patient management.

The first page of the program enables a quick overview over the course of the disease and treatment in case of disease progress. At each further control, changes in laboratory and clinical findings are described in the summary table.

There is a part of data in medical history with a questionable reliability because it refers to a very private information, *e.g.* age at first intercourse or number of partners.

Special part of the inquiry is dedicated to the signs and symptoms that are present at the presentation. Initially, many women with cervical cancer in early stages are asymptomatic, some have minor discharge or postcoital bleeding. With the progression of the disease symptoms change to purulent discharge due to tumour necrosis, compression symptoms (pain, hydronephrosis, renal failure etc.) and/or invasion symptoms (haematuria, haematochezia, or rectal bleeding).[11]

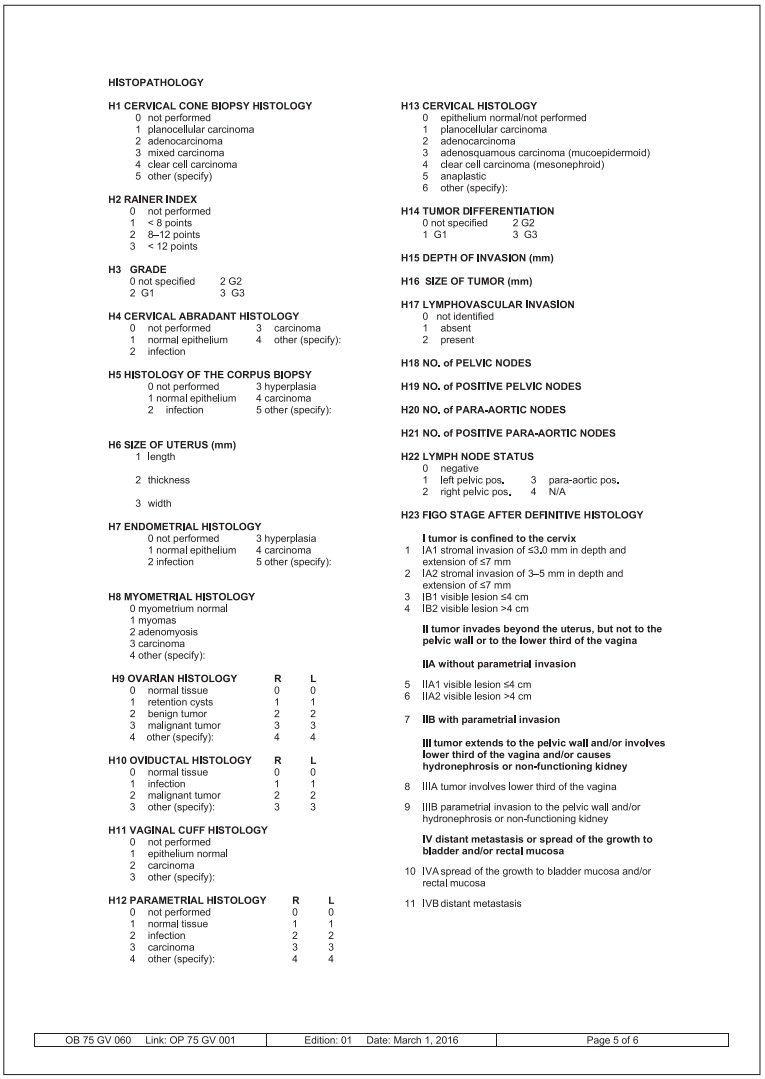
The duration of signs and symptoms is also recorded. Lim *et al.* found that 12 of the 27 women were diagnosed via symptomatic presentation with a median time from the symptom triggering presentation to presentation one month (interquartile range 0–4 months) and from presentation to diagnosis three months (interquartile range 1–8.5 months).[22] Patients who regularly attend gynaecologist appointments are, in all age groups, statistically significantly younger, the stage of cervical cancer at diagnosis is lower and are in higher percentage treated surgically.[23]

In the clinical examination section of the inquiry, the data of colposcopic, cytologic and HPV status of the patient are presented. Colposcopy is a subjective diagnostic method and a part of diagnostic work-up according to the Cervical Cancer Screening Programme ZORA guidelines.[24] High quality colposcopy is required and standardization is necessary. Any modifications of parameters in our inquiry are meaningful after standardization is done in a similar way that already exists for the cytology of cervix. Bethesda classification is used in the ZORA programme and in our inquiry. Cytology of the ZORA programme has the most elaborate quality control system.[25] It would seem reasonable to accept the changes agreed upon by the professional society.

The major etiological agent for developing cervical cancer is the high-risk human papillomavirus (HPV). The pre-vaccination prevalence of cervical infection in Slovenia with any hr-HPV type examined was 12.9%, with HPV 16 3.5%, and with HPV 18 1.0%.[26] The majority of HPV 16 and HPV 18 isolates together with HPV 11 and 33 belong to European branches.[27] HPV self-sampling among non-attenders to screening program can also show satisfactory results.[28]

Next part of the inquiry focuses on thorough external genital and vaginal examination, which should be performed during gynaecologic examination to define the extent of the disease and search for concomitant lesions. Therefore, vagina, uterine cervix and parametria are inspected and palpated.

The FIGO staging system for cervical cancer was modified in 2009 to define prognostic groups more accurately.[29] This staging was based mainly on clinical examination with the addition of certain procedures that were allowed by FIGO to change the staging. At the end of the chapter, FIGO preoperative stage is determined according to the revised 2018 FIGO staging system for cervical cancer which allows for imaging and pathological findings, where available, to assign the stage.[30]



HISTOPATHOLOGY

H1 CERVICAL CONE BIOPSY HISTOLOGY
0 not performed
1 planocellular carcinoma
2 adenocarcinoma
3 mixed carcinoma
4 clear cell carcinoma
5 other (specify)

H2 RAINER INDEX
0 not performed
1 < 8 points
2 8–12 points
3 < 12 points

H3 GRADE
0 not specified 2 G2
1 G1 3 G3

H4 CERVICAL ABRADANT HISTOLOGY
0 not performed 3 carcinoma
1 normal epithelium 4 other (specify):
2 infection

H5 HISTOLOGY OF THE CORPUS BIOPSY
0 not performed 3 hyperplasia
1 normal epithelium 4 carcinoma
2 infection 5 other (specify):

H6 SIZE OF UTERUS (mm)
1 length
2 thickness
3 width

H7 ENDOMETRIAL HISTOLOGY
0 not performed 3 hyperplasia
1 normal epithelium 4 carcinoma
2 infection 5 other (specify):

H8 MYOMETRIAL HISTOLOGY
0 myometrium normal
1 myomas
2 adenomyosis
3 carcinoma
4 other (specify):

H9 OVARIAN HISTOLOGY	R	L
0 normal tissue	0	0
1 retention cysts	1	1
2 benign tumor	2	2
3 malignant tumor	3	3
4 other (specify):	4	4

H10 OVIDUCTAL HISTOLOGY	R	L
0 normal tissue	0	0
1 infection	1	1
2 malignant tumor	2	2
3 other (specify):	3	3

H11 VAGINAL CUFF HISTOLOGY
0 not performed
1 epithelium normal
2 carcinoma
3 other (specify):

H12 PARAMETRIAL HISTOLOGY	R	L
0 not performed	0	0
1 normal tissue	1	1
2 infection	2	2
3 carcinoma	3	3
4 other (specify):	4	4

H13 CERVICAL HISTOLOGY
0 epithelium normal/not performed
1 planocellular carcinoma
2 adenocarcinoma
3 adenosquamous carcinoma (mucoepidermoid)
4 clear cell carcinoma (mesonephroid)
5 anaplastic
6 other (specify):

H14 TUMOR DIFFERENTIATION
0 not specified 2 G2
1 G1 3 G3

H15 DEPTH OF INVASION (mm)

H16 SIZE OF TUMOR (mm)

H17 LYMPHOVASCULAR INVASION
0 not identified
1 absent
2 present

H18 NO. of PELVIC NODES

H19 NO. of POSITIVE PELVIC NODES

H20 NO. of PARA-AORTIC NODES

H21 NO. of POSITIVE PARA-AORTIC NODES

H22 LYMPH NODE STATUS
0 negative
1 left pelvic pos. 3 para-aortic pos.
2 right pelvic pos. 4 N/A

H23 FIGO STAGE AFTER DEFINITIVE HISTOLOGY

I tumor is confined to the cervix
1 IA1 stromal invasion of ≤3.0 mm in depth and extension of ≤7 mm
2 IA2 stromal invasion of 3–5 mm in depth and extension of ≤7 mm
3 IB1 visible lesion ≤4 cm
4 IB2 visible lesion >4 cm

II tumor invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina

IIA without parametrial invasion
5 IIA1 visible lesion ≤4 cm
6 IIA2 visible lesion >4 cm

7 **IIB with parametrial invasion**

III tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney
8 IIIA tumor involves lower third of the vagina
9 IIIB parametrial invasion to the pelvic wall and/or hydronephrosis or non-functioning kidney

IV distant metastasis or spread of the growth to bladder and/or rectal mucosa
10 IVA spread of the growth to bladder mucosa and/or rectal mucosa
11 IVB distant metastasis

FIGURE 5. Histopathology, International Federation of Gynecology and Obstetrics (FIGO) stage after definitive histology.

L = left; R = right

Patients' WHO Karnofsky performance status (KPS) is important for decisions regarding the intensity of the forthcoming treatment.[31]

Radiography of the lungs and the skeleton, as well as intravenous pyelogram are allowed for FIGO staging. Computed tomography and magnetic resonance imaging are not allowed for FIGO staging making the data comparison between resource-rich and resource-poor countries impossible. Cystoscopy and proctoscopy are allowed for staging purposes and can reveal a tumour spread into these organs categorizing the patient into the IVA stage with poor treatment results.[32]

KT9 CYCLE	1	2	3	4	5	6
KT10 DATE						
KT11 WEIGHT (kg)						
KT12 HEIGHT (cm)						
KT13 SURFACE (m^2)						
KT14 WELLBEING 0 satisfied 1 neutral 2 dissatisfied						
KT 15 EXAMINATION						
KT17 ULTRASOUND 0 NAD 2 hydronephrosis 1 tumor 3 other						
KT18 ABDOMINAL CT 0 NAD 2 tumor 1 hydronephrosis 3 other						
KT19 CHEST RADIOGRAPH 0 NAD 2 meta 1 hydrothorax 3 other						
KT20 PATHOLOGY LAB RESULTS (AST, ALT, gamma GT, etc.)						
KT21 SCC						
KT22 CEA						
KT23 S-creatinine (SC) KT24 creatinine clearance (CrCl)						
KT25 DOSE REDUCTION (%)						
KT26 REASON FOR REDUCTION 1 ↓L 3 liver dysfunction 2 ↓T 4 renal dysfunction						
KT27 CYTOSTATIC 1 (mg)						
KT28 CYTOSTATIC 2 (mg)						
KT29 CYTOSTATIC 3 (mg)						
KT30 G-CSF (dose)						
KT31 ANTIEMETIC (mg)						
KT32 VOMITING 0 no 2 6–10x 1 1–5x 3 > 10x						

OB 75 GV 060 Link: OP 75 GV 001	Edition: 01 Date: 1. 3. 2016	Page 6 of 6

FIGURE 6. Chemotherapy cycles.

CEA = carcinoembryonic antigen; G-CSF = granulocyte colony stimulating factor; NAD = nothing abnormal detected; SCC = squamous cell carcinoma antigen

The treatment part of the inquiry includes surgery, radiotherapy, chemotherapy, and hormonal therapy. Details about each type of treatment are listed in the Treatment section along with the most common complications.

Because many women with cervical cancer are premenopausal, hormone replacement therapy (HRT) after cervical cancer treatment is applied frequently. Increased awareness of the health benefits and harms of HRT for this patient group is needed among both professionals and women.[33]

Histopathologic results of pre-treatment and definitive post-surgical specimens are presented on a separate inquiry page. The two most common histologic subtypes of cervical cancer are squamous cell and adenocarcinoma. Endocervical adenocarcinomas (ECAs) are currently classified according to the 2014 WHO system, which is predominantly based on descriptive morphologic characteristics, considers factors bearing minimal etiological, clinical, or therapeutic relevance, and lacks sufficient reproducibility.[34] Therefore, the 2017 International Endocervical Adenocarcinoma Criteria and Classification (IECC) system was developed by a group of international collaborators to address these limitations.[35]

The diagnosis of micro-invasive carcinoma can only be done after a careful histological examination of the specimen, when all damage is included and the incision into healthy tissue was made.[36] According to Copeland *et al.*, the risk of progression of micro-invasive cancer (invasion depth <3 mm) is 4.4 times higher in case of vascular invasion.[37] Detailed description of the histopathological biopsy and surgically retrieved specimens is described by Cibula *et al.* and includes all aspects of contemporary management of cervical cancer patients.[38] Standardization of histopathology is crucial, because it represents the foundation for staging and consequent treatment.[38-41] Regarding recent publications and Slovenian recommendations an upgrade of Cervix-Online in some segments *e.g.* histopathology would be appropriate.[40]

Survival is worse if cancer is diagnosed at advanced stage; and since in countries with high quality cervical cancer screening programmes majority of cancers in screening responders is prevented, most cancers that still do occur are in non-responders that are expected to be diagnosed at advanced stages, thus have worse survival overall. In a EUROCARE-5 study by Bielska Lasota *et al.*, worse survival in Eastern Europe was attributed to the fact that fewer or inadequate resources being allocated to health care in this area compared to the rest of Europe.[42] The medium time to recurrence is 7 to 36 months after primary treatment, so a closer clinical follow-up in the period of 2–3 years after treatment may be crucial with routine follow-up visits every 3–4 months for the first 2–3 years, followed by 6-monthly visits for 5 years, and then annually for life.[43] At each visit, history taking and clinical examination are carried out to detect treatment complications and psychosexual morbidity and to assess for recurrent disease.

Since original data are gathered in paper forms, possibility always exists of an overwriting error.

DATE	CERVIX	EXAMINATION A outpatient H hospital	WELLBEING 0 satisfied 1 neutral 2 dissatisfied	PAIN 0 absent 1 mild/minimal 2 moderate 3 severe	DISCHARGE 0 absent 1 minimal 2 moderate 3 severe	BLEEDING/FLOW 0 absent 1 minimal 2 moderate 3 severe	MICTION 0 normal 1 dysuria 2 polakisuria 3 incontinence 4 retention 5 fistula 6 other (details)	DEFECATION / BOWEL MOVEMENT 0 regular 1 obstipation/constipation 2 diarrhea 3 fistula 4 ileus 5 artificial anus (anus praeter) 6 other (details)	BODY WEIGHT (kg)	EXAMINATION 0 NAD 1 tumor (size) 2 hydronephrosis 3 kidney dysfunction 4 vaginal metastasis 5 pelvic metastasis 6 other metastasis 7 necrosis 8 fistula 9 lymphoedema 10 cachexia 11 other (details)	CERVICAL SMEAR 0 N/A 1 A 2 B 3 C ASC-US 4 C ASC-H 5 C LGSIL 6 C HGSIL 7 C SCC 8 C AGC-NOS 9 C AGC-neoplastic 10 C AIS 11 C AC 12 C SFM-NOS 13 C MLG-N 14 Non diagnostic	LAB 0 NAD 1 elevated SR 2 anemia 3 leukopenia 4 leukocytosis 5 thrombocytopenia 6 thrombocytosis 7 elevated SCC 8 elevated CEA 9 elevated creatinine 10 UTI 11 other (details)	CONDITION ASSESSMENT 0 alive, no symptoms 1 alive, partial remission 2 alive, stable disease 3 alive, relapse 4 alive, progressive disease 5 alive, condition unknown 6 ex due to cervix malignancy 7 ex during treatment 8 ex due to other disease, no cervical cancer 9 ex due to other disease, cervical cancer present 10 ex,cause unknown 11 condition unknown	NOTES
	BEFORE TH													
	MOS. AFTER TH													

FIGURE 7. Follow-up form.

TH = therapy; NAD = nothing abnormal detected; ASC-US = atypical squamous cells of undetermined significance; ASC-H = atypical squamous cells – cannot exclude HSIL; LGSIL = low-grade squamous intraepithelial lesion ; HGSIL = high grade squamous intraepithelial lesion; SCC = squamous cell carcinoma; AGC-NOS = atypical glandular cells not otherwise specified; AGC-neoplastic = atypical glandular cells, suspicious for AIS or cancer; AIS = adenocarcinoma in situ; AC = adenocarcinoma; SFM-NOS = suspicious for malignancy; MLG-N = malignancy; SCC = squamous cell carcinoma antigen; CEA = carcinoembryonic antigen; UTI = urinary tract infection

The filling out the form is always performed by a medical specialist to reduce this type of error.

Registries are a great source of data, but uncertainties about the quality of the data collected undermines confidence in the validity and reliability of the evidence generated. Incomplete or incorrect data entry might pose a limitation of the clinical registry, which depends on several healthcare professionals involved in the diagnostic procedures, treatment, and follow-up of cervical cancer patients.

Program Cervix-Online currently serves our needs because it allows for quick and easy data finding, listing and sorting, and the existing data can be modified or new data can be added, if necessary. Improvements are possible, in terms of standardization and particularly in the field of the quality management through quality planning, assurance, control and improvement.[44]

Connecting cervical cancer clinical registries to the Cancer Registry of RS as well as Cervical Cancer Screening registry ZORA within the ZORA programme into integrated health data space (like eHealth) would be very important in order to prevent multiplication of same data for same in fragmented information system, which is time consuming and prone to mistakes.

Conclusions

Cervical cancer is preventable and curable as long as it is detected early and managed effectively. The Global Strategy for cervical cancer elimination was

adopted by the World Health Assembly in August 2020 with the goal of reaching and maintaining an incidence rate of below four per 100 000 women through vaccination, screening and treatment.[45] The clinical cervical cancer registry plays a vital role in evaluating clinical practice in order to improve clinical work organization and the treatment of the disease. It allows us to continuously compare treatment results with national and international standards. The data can also be used for research projects and studies on cancer survival.

The Cervix-Online computer program allows for rapid and reliable processing and analysis of 116 different data obtained from cervical cancer patients, *i.e.* general information, medical history, diagnostics, treatment, and follow-up.

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