Evaluation of diagnostic accuracy and characteristics of operated cervical cancer patients in Lithuania 1998–2000

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Key words: *cervical cancer, diagnostic work-up, clinical staging, pathological staging.*

Summary. *The total number of new cases of cervical cancer for the three-year period was 1392 patients.The number of cases was fairly evenly distributed among the years of the study period 1998–2000. The total number of new cases of Stages I and II of cervical cancer was 713 (51.2%) cases, and that of Stages III and IV was 623 (44.8%) cases. The number of the new cases with an unknown stage of the disease was found to be 56 (4.0%) cases. The number of patients with Stage IIIB disease was the highest (69 cases) among all the stages of cervical cancer for the study period 1998–2000. The second most common stage was Stage IB disease with 52 patients belonging to this category. One-half (50.0%) of all operated patients because of cervical cancer during the study period 1998–2000 were women of 44 years of age and younger. Therefore, major considerations are to be given for women of reproductive age where effective screening and early detection of cervical pathology could help to avoid a lot of invasive cases of the disease and thus decrease mortality due to it. Generally, the diagnostic work-up and examinations of cervical cancer patients were insufficient, especially in cases of advanced stage disease. Stages III and IV were diagnosed in 44.8% of all cases. Overall, cystoscopy was performed in 39.4% (42 cases) of the total number of cases in Stages IIB through IVA of cervical cancer. Overall, rectosigmoidoscopy was performed in 6.4% (7 cases) of the total number of cases in Stages IIB through IVA of the disease. Finally, the proportion of CT that was performed in cases of Stages IIB through IVB of cervical cancer was 8.4% only.*

Clinical staging correlates well with pathologic staging in Stage I, particularly Stage IA (88.91%). The data also indicates that parametrial involvement would seem to be the most difficult problem, as 28.59% of Stage IIB and 32.3% of Stage IIIB were down-staged on the basis of pathological findings. This would suggest that in some cases the basic clinical staging rules are not being followed, or clearly understood. Kappa statistics (p=0.05), diagnostic agreement 86.9% ± 8%.

Introduction

Accurate tumor staging is crucial for appropriate therapy. Although there are numerous prognostic factors that may affect treatment planning, clinical International Federation of Obstetrics and Gynecology (FIGO) staging for tumor extension is usually the main determinant in guiding therapy choices (1). The staging of cervical cancer is based on clinical evaluation. Studies accepted for FIGO stage assignment include pelvic examination, cervical cytology, colposcopy, cervical biopsy, cystoscopy, barium enema or proctosigmoidoscopy, chest, x-ray, intravenous pyelography, and computed tomography or magnetic resonance imaging.

Assessment for clinical staging is best made by pelvic and rectal examination, preferably under anesthesia. Cystoscopy or rectosigmoidoscopy may be considered for patients with Stage IIB-IVA disease or those with history of urinary or lower gastrointestinal tract disturbances. Patients should have complete peripheral blood evaluation, including hemogram, white blood cell count, differential, and platelet count, blood urea nitrogen, creatinine, uric acid, and liver function tests; and urinalysis.

The initial staging system proposed in 1929 by a subcommittee of the League of Nations was later revised in 1937 and 1950. These functions were to be over by FIGO (International Federation of Gynecology and

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Obstetrics) in collaboration with the WHO (World Health Organization) and the International Union Against Cancer. The staging recommendations were last revised in 1995 (2). The 1985 FIGO revision (1) categorized minimal microscopic stromal invasion as Stage IA, and invasion of 5 mm or less in depth or 7 mm or less in horizontal spread as Stage IA2. As revised in 1995 (3), Stage IA represents microscopic disease, and any clinically apparent case is classified as Stage IB. Stage IA is further divided as follows: IA1 - invasion up to 3 mm deep and 7 mm wide; IA2 - invasion between 3 and 5 mm deep and 7 mm wide. Stage IB is divided as follows: IB1 - lesions no greater than 4 cm in diameter. IB2 - lesions greater than 4 cm in diameter (2). A parallel TNM staging system has been proposed by the AJCC (American Joint Committee on Cancer Staging) (4). All histologic types are included. When there is a disagreement regarding the staging, the less-advanced stage should be selected for statistical purposes.

The FIGO staging system is based on clinical evaluation (inspection, palpation, colposcopy); roentgenographic examination of the chest, kidneys, and skeleton; and endocervical curettage and biopsies (5). Suspected invasion of the bladder or the rectum should be confirmed by biopsy. Bullous edema of the bladder and swelling of the mucosa of rectum are not accepted as definitive criteria for staging.

For a lesion to be classified as Stage IIIB, the tumor should definitely extend to the lateral pelvic wall, although fixation is not required. Patients with hydronephrosis or nonfunctioning of the kidney ascribed to extension of the tumor are classified as Stage IIIB, regardless of the pelvic findings.

Discrepancies between clinical staging and surgical findings occur in 38% of patients (6). Therefore, many clinicians use "unapproved" staging modalities for treatment planing. Six years ago, the GOG reported their results from the largest prospective evaluation of cervical cancer staging modalities. After FIGO staging was assigned, 264 women with stages IIB-IVA cervical cancer underwent computed tomography (CT), ultrasound, and lymphangiography and subsequent surgical staging to assess the overall accuracy of these clinical modalities. The GOG found that lymphangiography was the most accurate non-invasive diagnostic test. In another GOG report (a multivariate analysis of women treated for cervical cancer with radiation therapy), the most important variable for survival was the presence or absence of aortic lymph node metastases. The investigators concluded: "the GOG will continue to require aortic lymph node evaluation for studies in locally advanced cervical cancer"(7). Fortunately, considerable technological improvements have occurred in CT and magnetic resonance imaging (MRI). CT is probably the most commonly performed imaging modality for cervical cancer staging. Scheidler et al. (8) conducted a meta-analysis of 17 studies to compare the utility between lymphangiography, CT, and MRI for the assessment of lymph node status in patients with cervical cancer. Contradicting the results from the aforementioned GOG staging study, there was no significant difference in overall accuracy between lymphangiography, CT, and MRI (8). A new imaging modality is position emission tomography (PET), which for solid tumor imaging is based on the high glycolytic rate and relative glucose-6-phosphatase deficiency of cancers. With the use of FDG (2-(^{18}F) fluoro-2-deoxy-D- glucose) as the radiopharmaceutical, Rose et al (9) studied 32 patients with FIGO stages IIB-IVA cervical cancer before planned aortic lymphadenectomy was performed. The sensitivity and specificity of PET scan assessment of the aortic lymph nodes were 75% and 92%, respectively. Interestingly, 1 of 2 patients with a false-negative PET scan had only one microscopic focus of metastatic disease (10).

The aim of this study is to evaluate the diagnostic accuracy and characteristics of operated cervical cancer patients at the main health care centers in Lithuania during the period 1998-2000.

Study objectives:

1. To perform an analysis of the operated patients at the main health care centers – Kaunas Medical University Hospital, Kaunas Oncology Hospital, and Lithuanian Oncology Center.
2. Evaluation of the diagnostic work-up of operated patients during the study period 1998-2000.
3. Compare cervical cancer diagnostic accuracy between the clinical staging (cTNM) and the surgical-pathological staging (pTNM) using correlation analysis.

Methods

Data about the patients was collected from January 1998 to December 2000 in systematic way during author's residentship at Kaunas University of Medicine, Department of Obstetrics and Gynecology. The agreements with the Departments of Gynecologic Oncology were made with the other two centers – Kaunas Oncology hospital and Lithuanian Oncology center to get access to the medical records of operated patients for study purposes. The database was designed for the study covering the following items as shown in Table 1 below.

The data collection form was designed in such a structure to cover the main issues of this study. The clinical details that were recorded for each patient were

Table 1. **The data base items to study the patients' characteristics and the clinical material at health care centers 1998-2000.**

Items	Comments	Notes
Date of birth	To calculate age of patient at operation	
Date of admission	Date of admission to health care center	
Place of residence	City or district	
Symptoms	Vaginal bleeding, contact bleeding, intermenstrual bleeding (acyclic), pain, urination disorders	
Cytology	Pap smear findings	
Rectovaginal examination	Positive findings	
Colposcopy	Colposcopic findings	
Histology	Technique of biopsy and histology findings	Punch biopsy, electrocautery biopsy, cone biopsy
Ultrasound examination	Abdominal or vaginal	Notes on abnormal findings
Chest X-ray findings	Present or absent	Notes on abnormal findings
Cystoscopy	Present or absent	Notes on abnormal findings
Rectosigmoidoscopy	Present or absent	Notes on abnormal findings
Computed tomography	Present or absent	Notes on abnormal findings
CTNM, pTNM	Extent of disease	Clinical and surgical (pathological) staging

the following: age at the time of operation to evaluate the mean age of the study group and its distribution by the stage of cervical cancer; place of residence to assess the effect of the geographical access of patients to the health care centers.

In addition to this, data on the diagnostic methods and imaging techniques were reviewed at the study. The medical records at each health care center were carefully studied taking into account the following: the presenting symptoms of the disease were recorded and classified into five groups reflecting the extent of the disease to a certain degree; the patients were evaluated at each health care center by the attending gynecologist who performed the rectovaginal examination to evaluate the local spread and the clinical stage of the disease, these procedures were recorded almost for all the study group patients from the medical records at each of the centers. Besides, data on the cytology, colposcopy, and histology reports were collected either from the medical records of the patients, or from the pathology department at each hospital.

Data on ultrasound examination, chest X-ray, cystoscopy, rectosigmoidoscopy, and computed tomography were collected from the medical records of the study group patients, and it was recorded the presence or absence of these studies, and in case of pathological findings detailed notes were taken.

The above-mentioned data make the diagnostic work-up of cervical cancer patients to define the clinical stage of the disease and perhaps the treatment of choice for every patient. The staging of cervical carcinoma is according to the classification of the International Federation of Gynecology and Obstetrics (FIGO) and TNM classification. The Staging procedure was based on carefully clinical evaluation by two gynecologists.

At last, data on the surgical-pathological staging (pTNM) were collected to compare with the clinical staging. The data on clinical staging were reviewed either from the medical records of patients at each center and from the Lithuanian Cancer Registry in Vilnius.

Table 2. **New cases of cervical cancer by stage in Lithuania 1998-2000**

Year	Stage				Unknown	Total
	I	II	III	IV		
1998	87	142	177	34	25	465
1999	88	131	170	50	20	459
2000	86	179	143	49	11	468

Statistical methods

The data were analyzed using descriptive and analytical methods. Quality checking and one or two-way tabulations were performed by MsExcell. The main statistical calculations were performed using statistical package "Statit Professional" (evaluation version) using the following statistical tests:

1. Confidence interval analysis test, statistically significant conclusions were obtained by checking the 95% range of the confidence interval.
2. T-test, statistically significant conclusions were obtained at p value less than or equal 0.05.
3. Chi-square test, statistically significant conclusions were obtained at p value less than or equal 0.05.
4. Diagnostic accuracy was estimated as correlation percentage between pre-operative and post-operative characteristics. The diagnostic agreement was tested by Kappa statistics. Statistically significant conclusions were obtained at p value less than or equal to 0.05.

Results

Population-based cervical cancer data was used from published sources and also from Lithuanian Cancer Registry. Number of new cases according to the stage of disease in Lithuania during 1998-2000 is represented in the table below.

Table 2 presents the distribution of new cases of cervical cancer by stage of the disease for the study period 1998- 2000. The total number of new cases of cervical cancer for the three-year period was 1392 patients. The number of cases is fairly evenly distributed among the years of the study period i.e. 1998-2000. The percentage of the new cases of cervical cancer was 33.4%, 33.0%, and 33.6% for the years 1998, 1999, and 2000 respectively. However, the distribution of the new cases by stage differs from one year to another. Stage I disease has an even distribution among the years of the study period, and it was approximately 87 new cases per year or a total of 261 (18.7%) cases for the years 1998-2000. Moreover, Stage II disease made-up a total of 452 (32.5%) new cases of cervical cancer, with a peak noticed in the year 2000 when Stage II disease was approximately 40.0 % of the total number of new cases of Stage II disease during the study period. However, a marked increase in the number of new cases of Stage III disease was noticed. Stage III disease made-up the largest amount of the new cases of cervical cancer and reached to a total of 490 (35.2%) cases during the study period 1998-2000. The peak for Stage III disease was noticed in the year 1998 when it made-up 36.1% (177) of the total number of new cases of this stage. Besides, the new cases of Stage IV disease made-up a total of 133 (9.5%) cases during the study period 1998-2000, with the lowest proportion of this stage (25.6%) was for the year 1998. The number of the new cases with an unknown stage of the disease was found to be 56 (4.0%) cases. Therefore, the total number of new cases of Stages I and II of cervical cancer was 713 (51.2%) cases, and that of Stages III and IV was 623 (44.8%) cases for the study period 1998-2000.

Table 3. **Number of operated patients by health care centers 1998-2000 and national coverage**

Center	Number of operated patients	Coverage, % of national cases (n=1392)
KMUH	39	2.8 (2.03÷3.85)
KOH	127	9.12 (7.69÷10.79)
LOC	180	12.9 (11.24÷14.83)
Total	346	24.8 (22.62÷27.23)

Patients' data was collected from three centers – Kaunas Medical University Hospital (KMUH), Kaunas Oncology Hospital (KOH) and Lithuanian Oncology center (LOC) - covering the period 1998-2000. All operated cases were examined and data was summarized in the designed study form for data collection. The size of the study group and the national coverage is represented in the table below.

Table 3 summarizes the total number of operated patients because of cervical cancer, and their distribution in the main health care centers in Lithuania - Kaunas Medical University Hospital (KMUH), Kaunas Oncology Hospital (KOH), and Lithuanian Oncology Center (LOC).

Table 4. **Health care centers and patient catchments areas**

Center	Place of residence					Total
	Vilnius and Vilnius region	Kaunas and Kaunas region	Klaipėda and Klaipėda region	Šiauliai	Panevėžys	
KMUH	1	36	1	0	1	39
KOH	1	122	1	2	1	127
LOC	96	15	32	8	29	180
Total	98	173	32	10	31	346

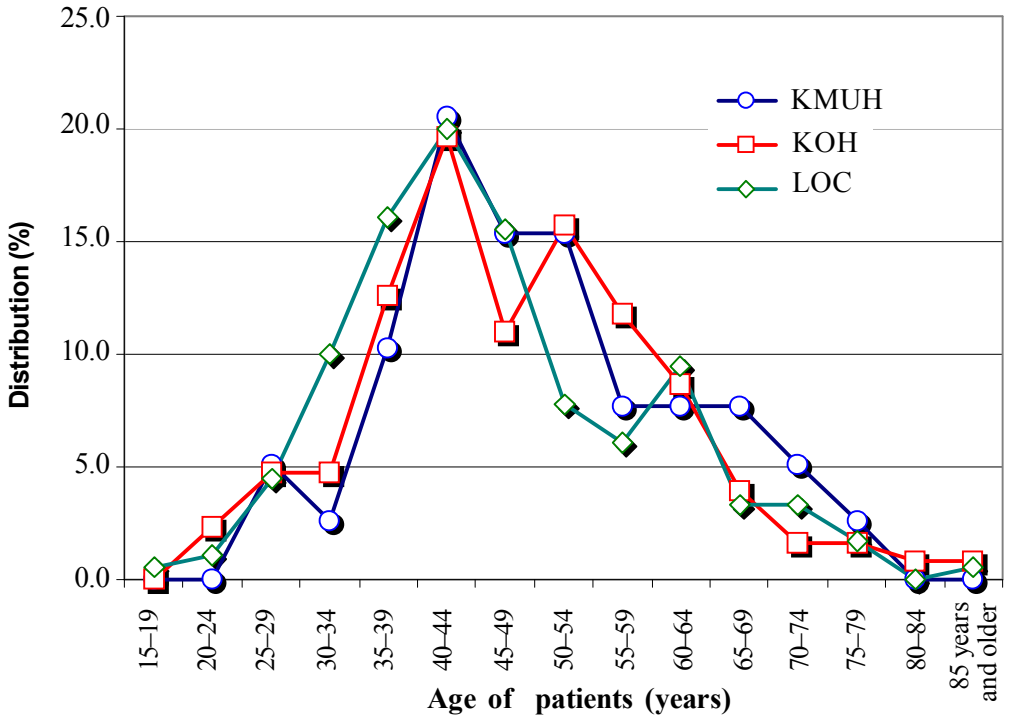

Fig. 1. **Distribution of patients by health care center and age**

The differences in the distribution of patients by age groups at the health care centers were not statistically significant (chi square (χ^2) test, $p>0.05$, $p=0.076$).

The total number of operated patients was 346 or 24.8 % of the total number of new cases of cervical cancer for the study period 1998-2000. This number of patients constitutes the target group of the present study. The major number of patients were operated at LOC, and it made-up 52.0% of the total number of operated patients among the health care centers for the years 1998-2000. In addition to this, the patient catchments areas for the health care centers mainly depend on the geographic relevance of the health care centers and the corresponding regions as shown in Table 3. However, LOC is an exception because 46.7% (84 cases) of its operated patients were referred from different regions other than Vilnius and its region as shown in Table 4.

Figure 1 present the distribution of patients by health care centers and age. The numbers of patients in the age groups 30-34 through 55-59 are evenly distributed among the health care centers. In addition to this, 71.8 % (28), 74.8% (95), and 75.0 % (135) of the total number of operated patients at KMUH, KOH, and LOC respectively belong to the age groups 30-34 through 55-59 years. However, the patients in the age group 15-19 years are present only at LOC, whereas, patients in the age group 80-84 at KOH only. To sum up, the distribution of patients by age among the health care centers is

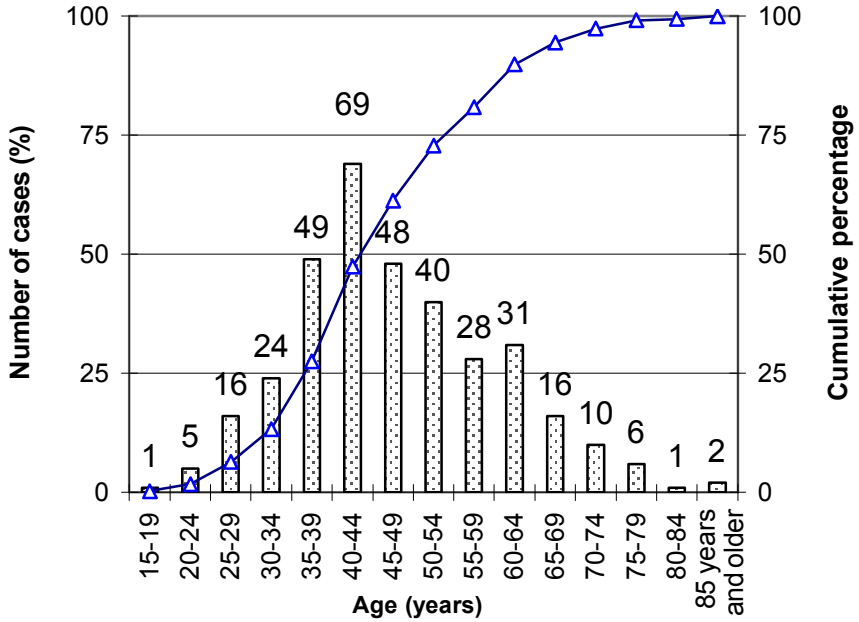

Fig. 2. **Percentage of cervical cancer cases by age groups**

Table 5. **Patients age characteristics by health care centers**

Center	Number of patients	Mean age (years)	Minimum	Maximum	CI, %.
KMUH	39	49,7	25	79	45.6–53.9
KOH	127	48,1	22	88	45.9–50.3
LOC	180	46,3	19	87	44.4–48.2
Total	346	47,7	19	88	46.0–48.7

not statistically significant (chi-square test, $p>0.05$, $p = 0.076$).

Figure 2 shows that one-half (50.0%) of all the operated patients because of cervical cancer during the study period 1998-2000 are women of 44 years of age and younger. However, the proportion of patients who are older than 55 years of age made up only 25% of the total number of cases. On the other side, 25% of all cases were women up to 35 years old. Overall, 25% of cases belong to the age groups 35-39 and 40-44 years.

Table 5 presents the mean age distribution by health care centers for the 346 operated patients during the study period 1998-2000. The mean age for all operated patients was 47.7 years, compared with 49.7 years for patients operated at KMUH, and 46.3 years for patients operated at LOC. However, 95% CI (confidence intervals) showed no significant differences for age distribution by health care centers.

95% CI of the mean age by health care center is overlapping - no significant differences for age distribution by health care centers.

Figure 3.a presents the mean age distribution by stage for the 346 operated patients during the study period 1998-2000. Mean age for Stage I disease was 46.2 years, and that of Stage II disease was 47.2 years. However, patients with Stage III disease had a mean age of 45.4 years, and it was the lowest mean age among all stages of the disease. Besides, the mean age of Stage IV disease was 46.5 years. This figure shows also a clear trend for the diagnosis of an advanced stage of the disease among the young-age groups.

Figure 3.b presents the numbers of patients by stages of the disease. The number of patients with Stage IIIB disease was the highest (69 cases) among all the stages of cervical cancer for the study period 1998-2000. The second most common stage was Stage IB disease with 52 patients belonging to this category. On the other hand, the lowest numbers of patients were three and one distributed between the Stages IIIA and IVA of the disease respectively.

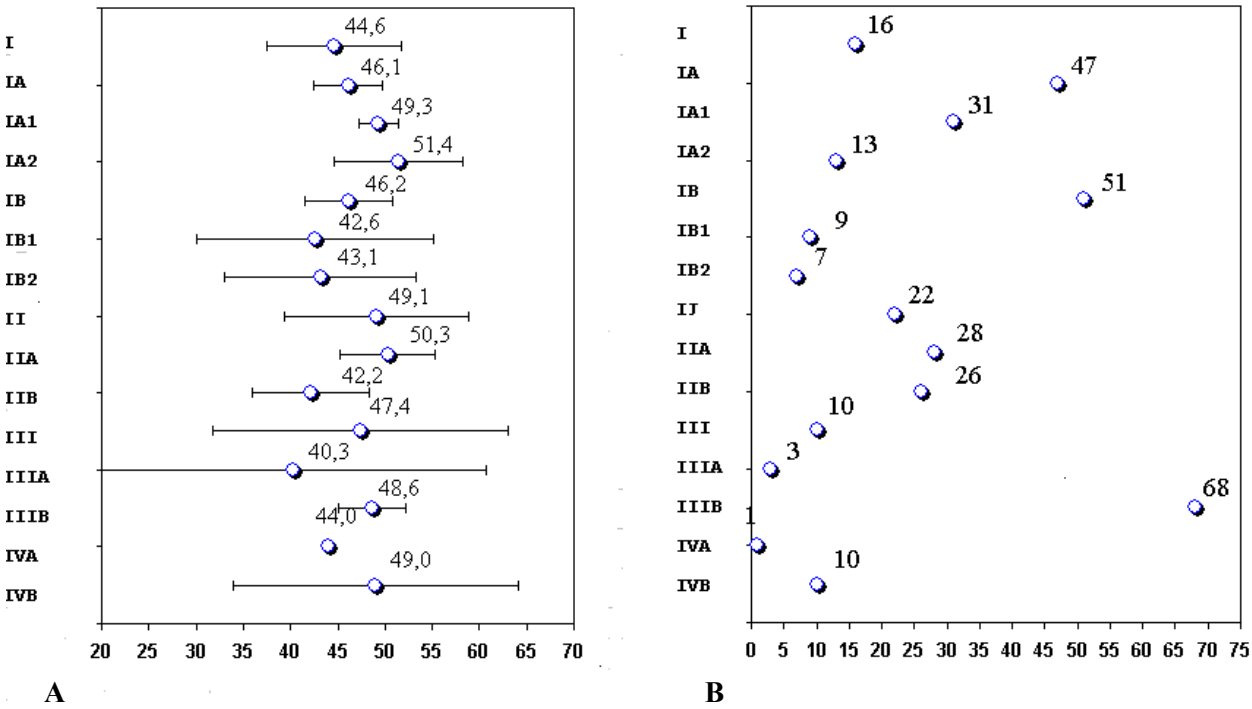

Fig. 3. **Patients distribution by stage: A - mean age, B - number of patients**

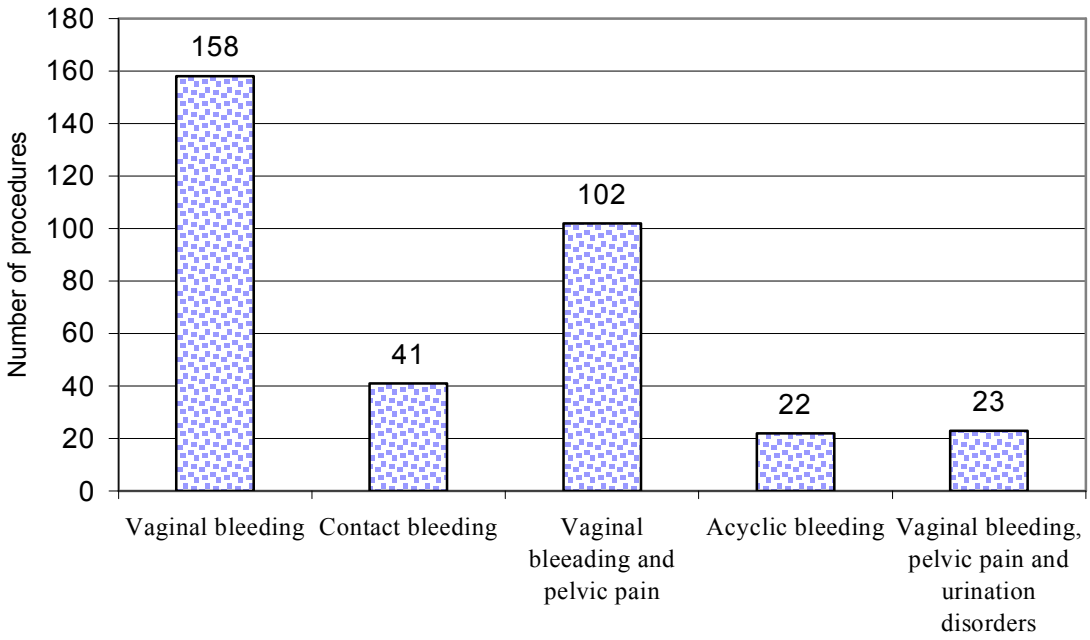

Fig. 4. **Distribution of the symptoms by the number of patients operated because of cervical cancer during the study period 1998-2000**

Diagnostic work-up of the operated patients during the study period 1998-2000.

Figure 4 shows that vaginal bleeding alone was the most common symptom among the 346 operated patients during the study period 1998-2000. The number of patients presented with only vaginal bleeding was 158 patients or 45.7% of the total number of patients. The second most common symptoms among these patients were

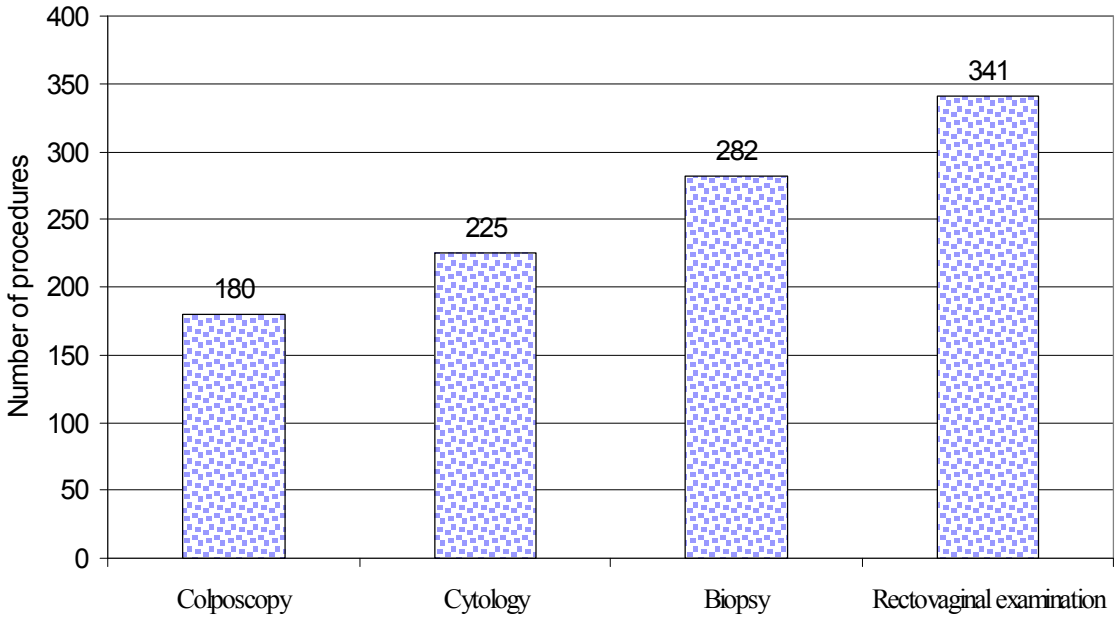

Fig. 5. **Carcinoma of the cervix uteri: Patients treated in 1998-2000. Distribution of the diagnostic procedures performed by the number of patients**

vaginal bleeding and pelvic or abdominal pain, and these symptoms were present in 102 patients or 29.5% of the total number of cases. In addition to this, contact bleeding (postcoital or after the gynecological examination) was present in 41 patients (11.8%) only. However, the number of patients having acyclic i.e. intermenstrual bleeding and those having symptoms of vaginal bleeding, pelvic pain, and urination disorders were almost evenly distributed among the 346 patients in proportions of 6.4% (22 cases) and 6.6% (23 cases) respectively. To sum up, approximately one-half of all the patients had only vaginal bleeding at the time of diagnosis.

Distribution of the symptoms differed among the stages of the disease. Overall, it was noticed that in all stages of cervical cancer there were dominance of only one symptom in 221 cases or 63.9% of the total number of operated patients. However, the presence of a group of symptoms together also was noticed to be present among the various stages of the disease in a proportion of 36.1% (125 patients) of cases. Generally, the presence of only one symptom was most common in Stage I and Stage II disease in proportions of 76.8% (136 cases) and 53.9% (41 cases), respectively of the total number of patients in each stage. However, the presence of more than one symptom was mostly in Stage III and Stage IV of the disease in proportions of 51.2% (42 cases) and 63.6% (7 cases) respectively.

Figure 5 shows that rectovaginal examination was the most common performed procedure among the 346 operated patients. The number of performed rectovaginal examinations was 341 or 98.6% of the total number of patients. On the other side, the least common procedure performed for the study group patients was colposcopy, and the number of cases who had this procedure was 180 only or 52.0% of the total number of cases. In addition to this, biopsies (punch biopsy or cone biopsy) and cytologic smears (Pap smear) were performed in proportions of 81.5% (282 cases) and 65.0% (225 cases) respectively.

Table 6. **Correlation percentage between cervical cytology and biopsy**

Biopsy	Cytology	
	Adeno Ca, %.	Squamous Ca, %.
Adeno Ca	**81.8**	18.2
Squamous Ca	1.1	**76.1**

Table 7. **Diagnostic accuracy between colposcopy and cytology**

Cytology	Colposcopy		Total
	positive	negative	
Positive	106	14	120
Negative	36	7	43
Total	142	21	163

Overall accuracy – 69.3±7.6 proc., p=0.055 (Kappa statistics).

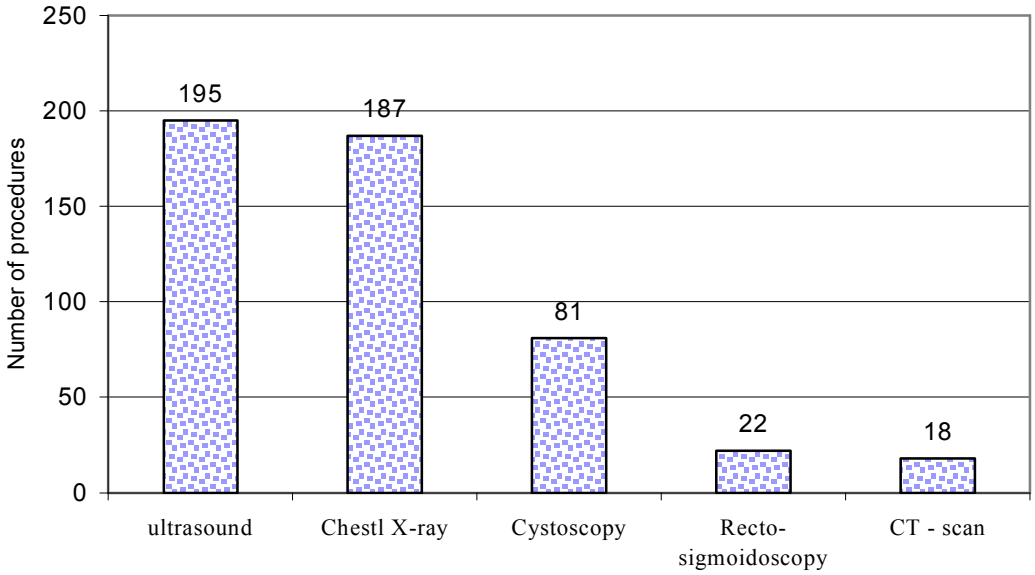

Fig. 6. **Carcinoma of the cervix uteri: Patients operated in 1998-2000. Distribution of the diagnostic procedures and imaging by the number of patients**

Overall, the diagnostic procedures were performed most commonly in cases of Stage I disease. The proportions of colposcopic procedures, cytologic smears, biopsies, and rectovaginal examinations were 63.3% (112 cases), 73.4% (130 cases), 95.0% (168 cases), and 98.9 % (175 cases) respectively in cases of Stage I disease.

Table 6 shows the correlation percentage between cervical cytology and histology in diagnosing cervical cancer. Overall, 197 cases were compared and the diagnostic accuracy for cervical cancer between the two methods was 95.0% and 74.6% for cervical biopsy and cytology respectively.

Table 7 presents the concordance in diagnosing cervical cancer between colposcopy and cervical cytology. Overall, 163 cases of colposcopy and cervical cytology reports were compared for the same patients. Generally, the diagnostic accuracy was present in 69.3% of these cases. However, colposcopic findings were more accurate to a certain extent where 87.1% of cases were positive for cervical malignancy; whereas, cytologic smears were positive in 73.6% only. To sum up, both methods are of important value in detecting cervical cancer (p=0.055).

This figure shows that the standard radiographic study performed was chest radiography in a proportion of 54.0% only (187 cases) of the total number of patients. In addition to this, the diagnostic imaging techniques were used in proportions of 56.4% (195 cases) and 5.2% (18 cases) for ultrasound examination and computed tomography respectively. However, the invasive diagnostic procedures- cystoscopy and rectosigmoidoscopy were performed in 23.4% (8 cases) and 6.4% (22 cases) respectively, of the total number of cases. Analysis of the diagnostic procedures and imaging by stage showed that significant variations in the distribution were present. Overall, ultrasound examination was the most common, and the highest proportions were noticed in Stage IV disease (81.8%) and Stage III disease (73.2%), in comparison to 45.8% in cases of Stage I disease. Besides, it is worth to mention that chest radiography was performed in proportions of only 64.6% and 55.3% in cases of Stage II and Stage III respectively. Overall, cystoscopy was performed in 39.4% (42 cases) of the total number of cases in Stages IIB through IVA of cervical cancer. In addition to this, rectosigmoidoscopy was performed in proportions of 8.5%, 7.9%, and 5.1% of the total number of cases in Stages III, II, and I respectively. Rectosigmoidoscopy was mainly performed in cases of Stage IIIA disease (33.3. Overall, rectosigmoidoscopy was performed in 6.4% (7 cases) of the total number of cases in Stages IIB through IVA of the disease. Finally, computed tomography was the least performed in cases of cervical cancer for the 346 operated patients during the study period 1998-2000. The proportions of CT were 27.3% in Stage IV and 7.3% in Stage III, in comparison to 3.9% and 3.4% in Stages II and I respectively. Besides, CT was performed in 30.0% of the cases of Stage IVB disease. Overall, the proportion of CT that was performed in cases of Stages IIB through IVB of cervical cancer was 8.4% only.

Tables 8 and 8 A compare the clinical stage in 298

Table 8. **Correlation percentage between pTNM (surgical-pathological) and cTNM (clinically assessed) in patients treated with surgery (surgery alone ± RT/CT)**

	PTNM, %.							
cTNM	**IA1**	**IA2**	**IB**	**IB1**	**IB2**	**IIA**	**IIB**	**IIIB**
IA1	**88.91**	6.53	2.47	1.01	1.08	0.00	0.00	0.00
IA2	4.88	**83.12**	3.59	2.71	1.70	1.71	2.29	0.00
IB	2.83	4.17	**83.30**	4.47	2.12	1.01	1.32	0.68
IB1	1.89	2.41	2.64	**80.19**	7.89	3.11	3.07	0.71
IB2	0.00	1.83	3.30	11.07	**67.83**	6.97	4.13	4.87
IIA	0.66	0.54	3.07	1.46	1.93	**63.90**	7.10	3.46
IIB	0.00	0.00	2.98	5.86	6.14	13.61	**57.53**	13.88
IIIB	0.00	0.00	2.39	4.18	4.26	11.60	9.87	**67.7**

Table 8 A. **Diagnostic accuracy and stage correlation between cTNM and pTNM**

Stage	Diagnostic accuracy, %	Stage-down, %	Stage-up, %
IA1	88.91	0.00	11.09
IA2	83.12	4.88	12.00
IB	83.30	7.00	9.70
IB1	80.19	6.99	12.87
IB2	67.83	16.20	15.97
IIA	63.90	7.66	28.44
IIB	57.53	28.59	13.88
IIIB	67.70	32.3	0.00

Table 9. **Diagnostic accuracy between local versus non-local extent of cervical cancer**

Extent of disease	cTNM	pTNM			Total	Diagnostic accuracy, %.
		localized	spread	advanced		
Localized	any T N0 M0	**242**	28	4	274	88.3
Spread	any T N1 M0	6	**11**	0	17	64.7
Advanced	any T, any N M1	2	0	**5**	7	71.4
Total		250	39	9	298	

Table 9 A. **Correlation percentage between pTNM and cTNM (clinically assessed) - local vs. non-local in patients treated with surgery (surgery alone ± RT/CT)**

Extent of disease	cTNM	PTNM, %.		
		localized	spread	advanced
Localized	any T N0 M0	**88.3**	10.2	1.5
Spread	any T N1 M0	35.3	**64.7**	0.0
Advanced	any T any N M1	28.6	0.0	**71.4**

patients with the surgical-pathological findings (pTNM). Clinical staging correlates well with pathologic staging in Stage I, particularly Stage IA1 (88.91%). The data also indicates that parametrial involvement would seem to be the most difficult problem, as 28.59% of Stage IIB and 32.3% of Stage IIIB were down-staged on the basis of pathological findings. This would suggest that in some cases the basic clinical staging rules are not being followed, or clearly understood.

Table 9 A presents the overall correlation between the local disease state and the spread to the lymph nodes or distant metastases. Clinical staging correlates well (88.3% with pathological staging in cases of local disease without spread to lymph nodes or distant metastases. However, 37.3% of the clinical cases that suggest nodal disease and 28.6% of the clinical cases that suggested distant metastases were down-staged to localized disease state after surgery.

Discussion

Characteristics of cervical cancer patients

Since 1960 associate professor Luchantas wrote about the early diagnosis and prevention of cervical cancer in Lithuania "all women according to their ages must have a systemic screening as the main way to decrease cancer diseases, and this is based on my data and that from literature" and "due to the dominance of the III and IV stages of cervical cancer the result of treatment is not satisfactory". The I and II stages of the disease were diagnosed only in 37.4 % of cases (11) in the state oncological hospitals for the years 1947-1954. In the last 40 years the situation had slightly changed. The diagnosis of the I and II stages of cervical cancer in Lithuania for the years 1994-1999 accounted only for 50% of all newly diagnosed cases.

During the study period 1988-2000, the total number of new cases of Stages I and II of cervical cancer was 713 (51.2%) cases, and that of Stages III and IV was 623 (44.8%) cases. The number of the new cases with an unknown stage of the disease was found to be 56 (4.0%) cases.

The number of patients with Stage IIIB disease was the highest (69 cases) among all the stages of cervical cancer for the study period 1998-2000. The second most common stage was Stage IB disease with 52 patients belonging to this category. On the other hand, the lowest numbers of patients were three and one distributed between the Stages IIIA and IVA of the disease respectively.

The age distribution of cervical cancer patients is bimodal, with peaks at 35 to 39 years and 60 to 64 years. Older women (age 60 and above) are at increased risk for cervical cancer as they are less willing or able to seek medical care for screening for this disease and participate in treatment. The mean age distribution by stage for the 346 operated patients was analyzed during the study period 1998-2000. Mean age for Stage I disease was 46.2 years, and that of Stage II disease was 47.2 years. However, patients with Stage III disease had a mean age of 45.4 years, and it was the lowest mean age among all stages of the disease. Besides, the mean age of Stage IV disease was 46.5 years.

In Lithuania the incidence rate of cervical cancer had decreased among older age women, however among young women it increased. One-half (50.0%) of all the operated patients because of cervical cancer during the study period 1998-2000 are women of 44 years of age and younger. However, the proportion of patients who are older than 55 years of age made up only 25% of the total number of cases. On the other side, 25% of all cases were women up to 35 years old. Overall, 25% of cases belong to the age groups 35-39 and 40-44 years. Therefore, major considerations are to be given for women of reproductive age where effective screening and early detection of cervical pathology could avoid a lot of invasive cases of the disease and thus decrease mortality due to it.

Clinical staging and diagnostic work-up of operated cervical cancer patients during the study period 1998-2000

Accurate tumor staging is crucial for appropriate therapy. Although there are numerous prognostic factors that may affect treatment planning, clinical International Federation of Obstetrics and Gynecology (FIGO) staging for tumor extension is usually the main determinant in guiding therapy choices (1). The staging of cervical cancer is based on clinical evaluation. Studies accepted for FIGO stage assignment include pelvic examination, cervical cytology, colposcopy, cervical biopsy, cystoscopy, barium enema or proctosigmoidoscopy, chest, x-ray, intravenous pyelography, and computed tomography or magnetic resonance imaging. Analysis of the diagnostic work-up of operated patients during the study period 1998-2000 revealed that, recto-vaginal examination was the most common performed procedure among the 346 operated patients. The number of performed recto-vaginal examinations was 341 or 98.6% of the total number of patients. On the other side, the least common procedure performed for the study group patients was colposcopy, and the number of cases who had this procedure was 180 only or 52.0% of the total number of cases. In addition to this, biopsies (punch biopsy or conization biopsy) and cytologic smears

(Pap smear) were performed in proportions of 81.5% (282 cases) and 65.0% (225 cases) respectively. Overall, the diagnostic procedures were performed most commonly in cases of Stage I disease. The proportions of colposcopic procedures, cytological smears, biopsies, and rectovaginal examinations were 63.3% (112 cases), 73.4% (130 cases), 95.0% (168 cases), and 98.9 % (175 cases) respectively in cases of Stage I disease.

The reason that Papanicolaou smear screening is so effective in preventing cervical cancer is that a precancerous lesion precedes the majority of cancers. This lesion may exist in the non-invasive stage for as long as 20 years and shed abnormal cells that can be detected on cytological examination (12). It is a matter of fact that cervical screening is absent in Lithuania, and due to this fact about one-half of patients presented with an advanced stages of the disease during the study period 1998-2000. Reliability of the smear depends on the technique employed to obtain the cytological specimen and the adequacy of its review by the cytologist. Papanicolaou smear failure rate in diagnosing invasive cancer is as high as 50 % (13) emphasizing the need to biopsy any visible lesions of the cervix, even if associated with a normal Papanicolaou smear. Careful inspection of the cervix and lower genital tract for areas of nodularity and friability should be part of each exam.

The standard radiographic study performed was chest radiography in a proportion of 54.0% only (187 cases) of the total number of patients. In addition to this, the diagnostic imaging techniques were used in proportions of 56.4% (195 cases) and 5.2% (18 cases) for ultrasound examination and computed tomography respectively. However, the invasive diagnostic procedures - cystoscopy and rectosigmoidoscopy were performed in 23.4% (8 cases) and 6.4% (22 cases) respectively, of the total number of cases. Overall, cystoscopy was performed in 39.4% (42 cases) of the total number of cases in Stages IIB through IVA of cervical cancer; rectosigmoidoscopy was performed in 6.4% (7 cases) of the total number of cases in Stages IIB through IVA of the disease. Finally, computed tomography was the least performed in cases of cervical cancer for the 346 operated patients during the study period 1998-2000. The proportions of CT were 27.3% in Stage IV and 7.3% in Stage III, in comparison to 3.9% and 3.4% in Stages II and I respectively. Besides, CT was performed in 30.0% of the cases of Stage IVB disease. Overall, the proportion of CT that was performed in cases of Stages IIB through IVB of cervical cancer was 8.4% only. Although the clinical staging system is useful for end-result reporting, for data comparisons, and for correlates with prognosis, it often inaccurate. Patients with early stage cervical cancer may be subjected to surgical intervention for what proves to be unresectable or metastatic disease. Patients with locally advanced cervical cancer may undergo inadequate radiation therapy because treatment fields do not encompass all areas of disease.

Nevertheless, clinical FIGO staging also has limitations. When correlated with surgical staging, clinical staging for cervical cancer has an error rate of 26-66 % (14). Magnetic resonance imaging, with superb soft tissue contrast and multiplanar capabilities, has been shown to be reliable in the evaluation of gynecological malignancies including cervical cancer (15). The diagnostic work-up of patients with cervical cancer was insufficient, especially in cases of advanced stage of the disease. The use of cystoscopy was only 36.6% and 32.9% of the total number of cases of stages IIIB and IIB respectively. Besides, computed tomography was used in 5.2% of the total number of operated patients during the study period 1998-2000. Besides MRI was not used for the clinical assessment of the disease.

In cervical cancer, tumor size has been regarded as an important prognostic factor correlating with the frequency of lymph node metastasis. Measurement of tumor size by palpation is unreliable and dependent on the experience of each clinician. Estimation of tumor size by CT scan is also less reliable because of relatively poor tissue contrast. Magnetic resonance imaging is considered to be a more reliable modality in measuring tumor size. In 85.3 % of the tumors larger than 1 cm, the discrepancy between the tumor size determined by MR imaging and the measured surgical specimens was < 5 mm (16).

The presence of lymph node metastasis has been shown to be an important prognostic factor for cervical cancer, yet it is not included in the clinical FIGO staging system (17). Cross-sectional imaging by CT and MRI has been advocated for the evaluation of lymph node status. The accuracy in the evaluation of lymph node metastasis by CT and MR is 83 and 88-90 %, respectively (18).

Cervical cancer stage correlation between clinical staging and surgical- pathological staging

Discrepancies between clinical staging and surgical-pathologic findings occur in about one third of patients, prompting several investigators to recommend pre-treatment surgical staging for patients at risk for aortic lymph node involvement (13,66). Perceived advantages to surgical staging include: (1) identification of clinically occult extrapelvic disease sites; (2) excision of inflamed adnexa or myomata, which otherwise may

complicate radiotherapy; and (3) down staging of patients to allow for more appropriate treatment (13). Pretreatment surgical staging would seem unnecessary for most early stage cervical cancers but is a consideration for stage IB2 (bulky) tumors, in which the incidence of positive aortic lymph nodes is 20% to 35% (19,20).

Clinical staging correlates well with pathologic staging in Stage I (79.4%). The data also indicates that parametrial involvement would seem to he the most difficult problem, as 33.3% of Stage IIIB was down-staged on the basis of pathological findings. Some other discrepancies are more difficult to explain, i.e. the 37.5% of clinical Stage IVA cases were down-staged to Stage I, and the 28.6% of clinical Stage IVB cases down-staged equally to Stages I and II after surgery. This would suggest that in some cases the basic clinical staging rules are not being followed, or clearly understood.

Overall, the correlations between the local diseases state and the spread to the lymph nodes or distant metastases showed that, clinical staging correlates well (88.3% with pathological staging in cases of local disease without spread to lymph nodes or distant metastases. However, 35.3% of the clinical cases that suggest nodal disease and 28.6% of the clinical cases that suggested distant metastases were down-staged to localized disease state after surgery.

Conclusions

1. During the study period 1998-2000, 1392 new cervical cancer cases were diagnosed and only 346 patients (24.8%, 95%CI=22.6-27.2) were operated at the main health care centers– LOC, KMUH and KOH. The 35-44 years age group had the highest proportion of operated cases, however, the distribution of patients by age among the health care centers was not statistically significant ($p>0.05$, $p=0.076$).

2. The stages of cervical cancer were unevenly distributed among the health care centers during the study period 1998-2000. The differences in the distribution are statistically significant ($p\leq0.001$). The distribution of the stages of cervical cancer at each health care center showed that, Stage IB disease, Stage IA disease, and Stage IIIB disease were the most common stages at KMUH, KOH, and LOC respectively. However, the advanced stages of the disease i.e. stages III and IV were most common at LOC, where 63.5% of the total number of these stages were present, in comparison with 29.0% at KOH, and only 7.5% at KMUH. The number of the new cases with an unknown stage of the disease was found to be 56 (4.0%) cases, and the total number of new cases of Stages I and II of cervical cancer was 713 (51.2%) cases, and that of Stages III and IV was 623 (44.8%) cases for the study period 1998-2000.

3. Generally, the diagnostic work-up and examinations of cervical cancer patients were insufficient, especially in cases of advanced stage disease. Stage III and IV were found in 44.8% of all cases. Overall, cystoscopy was performed in 39.4% (42 cases) of the total number of cases in Stages IIB through IVA of cervical cancer. Overall, rectosigmoidoscopy was performed in 6.4% (7 cases) of the total number of cases in Stages IIB through IVA of the disease. Finally, computed tomography was the least performed in cases of cervical cancer for the 346 operated patients during the study period 1998-2000. Overall, the proportion of CT that was performed in cases of Stages IIB through IVB of cervical cancer was 8.4% only.

4. Clinical staging correlates well with pathologic staging in Stage I, particularly Stage IA1 (88.91%). The data also indicates that parametrial involvement would seem to be the most difficult problem, as 28.59% of Stage IIB and 32.3% of Stage IIIB were down-staged on the basis of pathological findings. This would suggest that in some cases the basic clinical staging rules are not being followed, or clearly understood. Kappa statistics ($p<0.05$), diagnostic agreement 86.9% ± 8%.

Gimdos kaklelio vėžio diagnostikos metodų ir operuotų ligonių charakteristikos įvertinimas Lietuvoje 1998–2000 m.

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Raktažodžiai: gimdos kaklelio vėžys, diagnostika, klinikinė stadija, patologinė stadija.

Santrauka. Bendrasis naujų gimdos kaklelio vėžio atvejų skaičius per trejus metus buvo 1392. Atvejų skaičius tolygiai pasiskirstė per dvejus studijos metus. Bendrasis naujų I ir II stadijų skaičius buvo 713 (51,2 proc.), o III ir IV stadijų – 623 (44,8 proc.). Daugiausia nustatytas IIIB stadijos vėžys (69). Antra pagal dažnį buvo IB

stadija, kuri nustatyta 52 pacientėms. Pusė (50,0 proc.) pacienčių buvo 44 metų ir jaunesnės. Taigi didžiausias dėmesys turėtų būti skiriamas reprodukcinio amžiaus moterims vykdant efektyvų tyrimą ir nustatant ankstyvąją gimdos kaklelio patologiją bei siekiant išvengti invazinės ligos atvejų ir su tuo susijusio mirtingumo. Pacienčių, sergančių gimdos kaklelio vėžiu, ištyrimas buvo nepakankamas, ypač esant vėlyvajai ligos stadijai. 44,8 proc. gimdos kaklelio vėžio buvo III ir IV stadijos. Cistoskopija atlikta 39,4 proc. (42 pacientėms) pacienčių esant IIB–IVA gimdos kaklelio vėžio stadijai. Rektosigmoidoskopija atlikta 6,4 proc. (7 pacientėms) pacienčių esant IIB–IVA stadijoms. KT atlikta tik 8,4 proc. pacienčių esant IIB–IVB stadijoms. Klinikinė ligos stadija sutapo su chirurgine ir patologine esant I ligos stadijai, ypač IA (88,91 proc.). Duomenys rodo, kad nustatytų parametrų įtraukimas yra sudėtingas, kadangi 28,59 proc. IIB stadijos atvejų, 33,3 proc. klinikinės IIIB stadijos atvejų sumažinta remiantis patologiniais radiniais. Tai reikštų, kad kai kuriais atvejais nesilaikoma pagrindinių klinikinės stadijos nustatymo principų arba jie nesuprantami. Diagnozės po operacijos sutapo 86,9±8 proc. (Kappa statistika, $p<0,05$).

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