Clinical audit of patients with cervical cancer in Slovenia. Data analysis from 2003-2006

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Summary

Purpose of Investigation: From 2003 to 2006 the data on Slovenian cervical cancer patients who regularly attended a gynecologist were gathered. Data were analyzed in order to improve the efficiency of the cervical cancer screening program. *Methods:* Data on all patients newly diagnosed with cervical cancer were collected at three central clinics in Slovenia. The results are a presentation and comparison of detailed information on some characteristics of cervical cancer patients of the group that regularly visited a gynecologist and of the other group who did not. Data were processed by descriptive epidemiological methods. Mantel-Haenzel χ^2 and Fisher's p tests were used to evaluate statistical significance. *Results:* On average, 55% of patients with cervical cancer underwent a gynecological examination five years before the diagnosis. The patients who regularly attended their gynecologist were, in all age groups, statistically significantly younger, the stage of cervical cancer at diagnosis was statistically significantly lower (p = 0.01) and were, in statistically significantly higher percentage, treated surgically (p < 0.01). From 2003 to 2006, each patient had on average five examinations at her gynecologist within the period of five years to six months before the diagnosis of cervical cancer. The average number of collected smear samples was 3.2. *Conclusion:* From the results of our analysis, it may be concluded that improvements are needed in Slovenia in the field of screening for and early detection of cervical cancer.

Key words: Clinical audit; Cervical cancer; State screening program; Premalignant cervical disease.

Introduction

In addition to a sufficiently large number of women recruited through screening, the most important measures to be taken to assure successful cervical cancer screening are effective detection of premalignant cervical disease and prompt, as well as high-quality, treatment. However, it is of key importance that all individual processes included in the entire screening program, such as data gathering and storing in the screening program registry and in the Cancer Registry of Slovenia, proper functioning of the information system, collection of cervical smear samples, treatment of cervical diseases, and follow-up treatment as well as the work in cytopathology laboratories, are running smoothly and in tune with each other. Had one of these processes included in the program not met the required quality criteria, others would not have been able to replace the resulting deficit, though they would have exceeded all quality standards with their extreme assiduousness [1, 2].

Hence, the success in screening for cervical cancer may hardly be expected if the quality control indicators of individual processes included in the multidisciplinary program are not regularly followed-up, if no critical analyses are performed, and if regular checks for eventual inadequacies of these processes and immediate corrective measures are not carried out. Very often, the availability of the results obtained from appropriate analyses may be of

great help in the endeavors to suppress the rate of shortcomings. At the same time, the staff working in the screening program should be given the chance to continuously improve their knowledge as well as to have access to the latest analysis results, the data on the proposed improvements, and the innovations carried out in specific fields within the program. The last is particularly important in case the staff in charge is performing highly subjective examination methods, i.e., cervical cancer smear tests and evaluation of colposcopic examination findings [3 ,4].

In Slovenia, systematic screening for cervical cancer was started in 1998. At first it was implemented as a pilot program and in 2002, as a national cervical cancer screening program aimed at reducing the cervical cancer incidence in Slovenia. The major reason that compelled us to start working within a highly organized and planned system rather than within an opportunistic program was the increasing cervical cancer incidence that was first observed after the year 1994. The incidence was the highest in 1997 (23.6/100,000), but after the year 1998, it dropped slightly to 20/100,000 [5]. The most recent data for the year 2004 showed that the cervical cancer incidence was still 19.1/100.000 (in 2003, 20.4/100,000). In 1994 and 1993, the CIN 3 incidence was 94.4/100,000 and 85.2/100,000, respectively [6].

To facilitate the evaluation of certain parameters applied in the national cervical cancer screening program in Slovenia, we started with gathering the data on Slovenian patients with cervical cancer who regularly attended a gynecologist, but despite that, contracted invasive cervical cancer. The gathered data were then analyzed to

find any deficiencies that would help us to improve the efficiency of the cervical cancer screening program and the detection of premalignant cervical disease.

Methods

In 2003, a research study was started on patients who were regularly attending a gynecologist and who were diagnosed with cervical cancer that same year. The data on all patients newly diagnosed with cervical cancer were collected at the same time at three clinics in Slovenia: Institute of Oncology Ljubljana, University Medical Centre, Department of Gynaecology and Obstetrics, Ljubljana, and University Medical Center Maribor, Clinic for Gynaecology and Perinatology, Maribor. The synchronous gathering of data on the patients with newly diagnosed cervical cancer in three clinics was chosen because we expected that we would thus have easier access to the data, better control over the then circumstances, and better chances of taking prompt and proper measures. Moreover, we also avoided the gathering of the data of deceased patients. The same method of data gathering was applied also in 2004, 2005, and 2006. The data were gathered through interviews with patients, from hospital files, and from the patients' questionnaires which were handed over to us by their gynecologists upon having obtained consent from the patients. A few patients who reported that they had not attended the appointment with their gynecologists despite having received an invitation were classified into the group of patients who did not attend gynecologists. From earlier analyses made by other authors from Slovenia on the data provided by cervical cancer patients, it could be assumed that the patients did not always supply the exact data on their visits to the gynecologists; this assumption could not be confirmed even by the present analysis [7].

The analysis results are a presentation and comparison of detailed data on some characteristics of cervical cancer patients of the group that regularly visited a gynecologist and of the other group who did not. In the second part, some screening data of the patients who regularly attended gynecologists are presented; these are the data on cervical smear test results, diagnostic procedures, and symptoms. The screening time covered by the analyses goes back to the period extending from five years to six months before the diagnosis.

In the years between 2003 and 2006, the total number of patients with detected cervical cancer was 585. Of 585 patients, 323 (55.21%) had visited a gynecologist in the last five years before the diagnosis (Table 1). The remaining 44.89% of patients did not visit their gynecologists, sometimes for 15 years or even more. Our results reconfirm the assumption made in our earlier paper that the women who do not regularly visit a gynecologist hardly ever make a decision on their own to visit a gynecologist for an examination. In the recent past, conization was performed in 7.43% of the cervical cancer patients who regularly attended a gynecologist and in 1.9% of those who did not (p < 0.01).

The data were processed by descriptive epidemiological methods. Mantel-Haenszel χ^2 and Fisher's p tests were used to evaluate statistical significance.

Table 1. — *Distribution of patients with cervical cancer by gynecological examinations performed within the last five years before the diagnosis of cervical cancer and the year diagnosis was established.*

Gynecological Examinations	2003	2004	2005	2006	Total	%
Yes	91	79	72	81	323	55.21
No	58	88	62	54	262	44.89
Total	149	167	134	126	585	100.00

Results

Age of patients, pathohistological status of cervical cancer, disease stage and therapy of the group of patients who regularly attended a gynecologist and of the other group who did not.

Mean age of the patients who regularly attended a gynecologist and of the other group who did not was 43.6 and 57.2 years, respectively. The patients who regularly attended a gynecologist were statistically significantly younger in all age groups than those of the other group who were not visiting a gynecologist. The percentage of patients aged ≥ 49 years in the group of patients regularly attending a gynecologist and of the other group who did not was 75.62% and 32.82%, respectively (p < 0.01). The percentage of patients aged ≤ 70 years in the group of patients who regularly attended a gynecologist and of the other group who did not was 2.74% and 21.76%, respectively (Table 2).

Table 2. — *Distribution by age and year diagnosis of cervical cancer was established in patients who visited (YES) or did not visit (NO) regularly a gynecologist.*

Age (years)	2003 Yes	2003 No	2004 Yes	2004 No	2005 Yes	2005 No	2006 Yes	2006 No	Total Yes	Total No	% Yes	% No	p
up to 29	9	0	5	0	4	0	5	1	23	1	7,21	0.38	< 0.01
30-39	29	5	22	5	26	9	24	7	101	26	31.26	9.92	< 0.01
40-49	32	16	27	10	26	20	35	13	120	59	37.15	22.52	< 0.01
50-59	11	15	19	27	10	9	10	8	50	59	15.47	22.52	0.03
60-69	8	11	3	29	4	11	5	9	20	60	6.14	22.90	< 0.01
70-79	2	8	2	11	2	7	2	10	8	36	2.47	13.74	< 0.01
80 or more	0	3	1	6	0	6	0	6	1	21	0.30	8.02	< 0.01
Total	91	58	79	88	72	62	81	54	323	262	100.00	100.00	

The most frequent carcinoma that was diagnosed in the patients included in our study in the period 2003 to 2006 was squamous cell carcinoma (80.86%), the second was adenocarcinoma (12.83%), and the third adenosquamous carcinoma (4.95%), followed by other types of carcinomas (1.36%). Adenocarcinoma was detected more frequently in the patients who regularly visited a gynecologist (15.78%) than in those who did not (9.16%; p = 0.01). Squamous cell carcinoma was statistically significantly more frequently detected in the patients who did not regularly visit a gynecologist (84.74%) than in those who did (77.69%); the difference was statistically significant (p = 0.02).

In the patients who regularly attended a gynecologist, the stage of cervical cancer at diagnosis was statistically significantly lower (p = 0.01) (Table 3). This difference is the most obvious in disease Stage I A. In patients who

Table 3. — *Distribution by stage and year of diagnosis of cervical cancer was established in patients who visited (YES) or did not visit (NO) regularly a gynecologist.*

Stage	2003 Yes	2003 No	2004 Yes	2004 No	2005 Yes	2005 No	2006 Yes	2006 No	Total Yes	Total No	% Yes	% No	p
IA	22	4	31	6	38	7	23	3	114	20	35.29	7.63	< 0.01
IB	60	18	33	37	27	22	55	19	175	96	54.17	36.64	< 0.01
II	8	12	7	12	5	10	1	5	21	39	6.50	14.88	< 0.01
III	2	20	6	29	1	16	2	20	11	85	3.40	32.44	< 0.01
IV	0	3	2	4	1	7	0	7	3	21	0.92	8.01	< 0.01
Total	91	56	79	88	72	62	81	54	323	262	100.00	100.00	

Table 4. — *Distribution of cervical smear test results by periods ranging from 6 to 60 months before diagnosis in the years 2003 to 2006.*

PAP result Period	Inadeq. smear	Neg.smear	Reactive changes	ASCUS or AGC	Mild dyskaryosis	Moderate or severe dyskaryosis	Suspic. or malignant cells	All	%
> 6 M till < 12 M	1 (1.56%)	16 (25%)	6 (9.37%)	13 (20.31%)	13 (20.31%)	14 (21.88%)	1 (1.57%)	64	100.00
12 M till < 24 M	4 (5.19%)	40 (51.95%)	2 (2.69)	13 (16.89%)	14 (18.18%)	3 (3.9%)	1 (1.30%)	77	100.00
24 M till < 36 M	2 (2.54%)	49 (62.02%)	7 (8.86%)	9 (11.39%)	8 (10.13%)	4 (5.06%)	0	79	100.00
36 M till < 48 M	5 (5.25%)	56 (57.83%)	5 (5.15%)	13 (13.40%)	6 (6.25%)	4 (4.12%)	0	97	100.00
48 M till < 60 M	4 (5.19%)	58 (75.33%)	4 (5.19%)	3 (3.9%)	7 (9.09)	1 (1.30%)	0	77	100.00

regularly visited a gynecologist and in those who did not, this disease stage was detected in 35.29% and in 7.63%, respectively. The comparison of the disease Stages IA1 and IA2 did not show statistically significant differences between the two groups (p = 0.69).

The differences between the two groups with regard to disease stage were also related to the selection of treatment modality. A statistically significantly higher percentage of patients who regularly visited a gynecologist were surgically treated more often (85.44%) than those who did not (38.16%; p < 0.01). Radiotherapy (with or without systemic treatment) was performed in 13.93% of patients who regularly visited a gynecologist and in 57.63% of those who did not (p < 0.01). Symptomatic treatment was applied in 0.63% of patients who regularly visited a gynecologist and in 4.21% of those who did not (p < 0.01).

Data on screening the patients who regularly visited a gynecologist: number of gynecological examinations, cervical smear test results, diagnostic procedures and symptoms.

From 2003 to 2006, each patient had on average five examinations at a gynecologist within the period of five years to six months before the diagnosis of cervical cancer (in 2003, 7.0 examinations; in 2004, 5.2 examinations; in 2005, 4.9; and in 2006, 3.6 examinations). The average number of collected smear samples was 3.2 (in 2003, 3.7; in 2004, 3.4; in 2005, 3.0; and in 2006, 2.8). On average, 55% of patients with cervical cancer had undergone a gynecological examination five years before the diagnosis.

In line with our expectations, the percentage of negative smear test results (75.33%) was the highest in the patients who were tested five years before the diagnosis of cervical cancer. In the following years, the percentage of negative test results gradually decreased; four years before the diagnosis of cervical cancer, the percentage of negative smear test results was 57.83%, three years before the diagnosis it was 62.02%, two years before 51.95%, and 7-12 months before the diagnosis, as much as 25% of patients still had negative test results (Table 4). On the other hand, the closer the date of the diagnosis, the more the percentage of pathologic cervical smear test results increased in inverse proportion to normal test

results. In the period of 7-12 months before the diagnosis, the percentage of moderate dyskaryosis was 23.45%. These smears most frequently tested positive for initial pathologic changes, such as ASCUS or AGNUS or mild dyskaryosis. Five years and 7-12 months before the diagnosis, 5.19% and 1.56% of collected smear samples, respectively, were inadequate (Table 4).

From 2003 to 2006, colposcopy was performed in 70.3% of patients, biopsy or curettage in 20.3%, and excision (LLETZ, cone biopsy) or destructive surgical techniques in 9% of patients. HPV tests were carried out in 4.85% of patients. More detailed data on diagnostic procedures performed within specific time periods before the diagnosis are presented in Table 5.

Table 5. — *Diagnostic procedures by periods ranging from 6 to 60 months before diagnosis in the years 2003 to 2006.*

Dgn procedure Period	Colposcopy	Biopsy, curettage	Excisional methods	Destructive methods	HPV test	Other	All	%
> 6 M till < 12 M	19 (73.07%)	3 (11.54%)	2 (7.69%)	0	1 (3.85%)	1 (3.85%)	26	100.00
12 M till < 24 M	17 (48.58%)	12 (34.28%)	1 (2.86%)	3 (8.57%)	2 (5.71%)	0	35	100.00
24 M till < 36 M	22 (70.78%)	8 (25.86%)	0	0	0	1 (3.36%)	31	100.00
36 M till < 48 M	15 (75.00%)	3 (15.00%)	0	1 (5.00%)	1 (5.00%)	0	20	100.00
48 M till < 60 M	11 (84.61%)	2 (15.39%)	0	0	0	0	13	100.00

Cervical diseases, e.g., premalignant cervical disease or cervical cancer, are accompanied by the development of certain discomforts. The patients who were diagnosed with cervical cancer had often complained to their gynecologist of the problems they had before the diagnosis. These disorders were already dealt with by our earlier studies; however, the data gathered in 2003 again demonstrated the occurrence of some clinical symptoms typical of cervical cancer that had been reported by the patients before the diagnosis. These symptoms described by the patients who regularly visited a gynecologist were different, depending on the time lapse until the diagnosis. Five years before the diagnosis the majority of women did not complain of any gynecological problems, three years before the diagnosis they reported vaginal discharge and

inflammation, and one year before the diagnosis they described symptoms typical of premalignant cervical disease or cervical cancer (Table 6).

Table 6. — *Symptoms by periods ranging from 6 to 60 months before the diagnosis in the years 2003 to 2006.*

Symptoms Period	Without	Inflammation	MTG	Mixture	Lumbar pain	Other	All	%
> 6 M till < 12 M	25 (50.00%)	10 (20.00%)	11 (22.00%)	1 (2.00%)	1 (2.00%)	2 (4.00%)	50	100.00
12 M till < 24 M	23 (42.59%)	16 (32.00%)	9 (16.66%)	0	0	6 (11.11%)	54	100.00
24 M till < 36 M	21 (51.22%)	14 (34.14%)	3 (7.31%)	1 (2.34%)	0	2 (4.87%)	41	100.00
36 M till < 48 M	27 (65.85%)	8 (19.51%)	2 (4.87%)	1 (2.34%)	0	3 (7.31%)	41	100.00
48 M till < 60 M	30 (96.77%)	3 (9.67%)	2 (6.45%)	0	0	3 (9.67%)	38	100.00

Discussion

The present study is an analysis of the data on patients with newly detected cervical cancer in the period between 2003 and 2006. Our main interest was to find out whether any changes in clinical data occurred within the four-year period of organized screening for cervical cancer in Slovenia.

No significant difference was observed between the years 2003 and 2006 in the percentage of patients who had a gynecological examination within the period of five years before the diagnosis of cervical cancer (please note that the examinations performed six months before the diagnosis with the aim of confirming the diagnosis were not included). In 2006 and in 2003, the percentages of the patients who had gynecological examinations within the period of five years before the diagnosis of cervical cancer were 57.9% and 60.0%, respectively. The data gathered throughout the period between 2003 and 2006 indicate a trend of a gradually increasing percentage of patients who had not visited a gynecologist or had not had cervical sample tests for 15 or more years. In the years 2003, 2004, 2005, and 2006, the percentages of these patients were 42%, 45%, 50%, and 44%, respectively. One fourth of the patients who had not been regularly visiting a gyneceologist had the gynecological examination within the period of less than ten years before the diagnosis (in 2006 and 2003, 22% and 29%, respectively).

In 2006, the mean age of all patients was 49.8 years, and in 2003, 48.2 years. In 2006 the majority of patients contracted cervical cancer at the age of 40-44 years, and in 2003 at the age of 45-49 years. One third of the patients included in these two observation periods were older than 50 years. The data from 2006 indicate a greater percentage of patients older than 69 years and of those aged between 30 and 34 years.

The mean age of patients who had a gynecological examination was statistically significantly lower than the mean age of the patients who were not visiting a gynecologist. Similar data are also reported in studies by other authors [8]. No statistically significant difference was observed between the years 2003 and 2006 in comparing the mean age of patients. However, the difference between the two years was obvious when comparing the mean age of the patients who were not regularly visiting a gynecologist; in 2006, the mean age of these patients was higher (58.6 years) than in 2003 (55.5 years). In both observation periods, the majority of the patients who were not regularly visiting a gynecologist were diagnosed with cancer at the age of 60-69 years.

The data on pathohistological findings also demand closer attention. A higher percentage of adenocarcinoma in the patients who regularly attended a gynecologist may support the hypothesis that the cervical smear test results of these patients have been indicating a pathological process in initial stages in the endocervix, but, due to insufficient diagnostic procedures, the pathological changes could not be detected. This assumption may be also confirmed by a high percentage of the disease detected in Stage I in patients who regularly visited a gynecologist. From the comparison of the data of 2003 and 2006, a gradual increase of the disease detected in Stage I and Stage IA was noted in patients who regularly attended a gynecologist, which could be an indication of a positive change resulting from effective screening and early detection of cervical cancer in Slovenia.

The average number of gynecological examinations and cervical smear tests performed in the patients with cervical cancer who visited a gynecologist within the last five years before the diagnosis dropped significantly in 2006, which is in line with the new recommendations for detecting, treating and following-up patients with premalignant cervical disease [11]. In 2006 the average number of gynecological examinations per patient was 3.6, while in 2003 it was 7.03. The number of cervical smear tests performed per patient in 2006 was 2.8, whereas in 2003 it was 3.7.

The percentage of our patients with consistently negative cervical smear test results is similar to the percentage reported by other authors [8-10]. A systematic and independent re-evaluation of negative cervical smear test results has not been made yet. The results also reveal a considerable number of cervical cancer patients who had negative cervical smear test results a few years before the diagnosis. Atypical glandular cells are still a frequent result of cervical smear tests in patients who later develop glandular cervical cancer. With regard to some new developments observed in cervical smear test results, certain changes will be introduced in diagnostic procedures, such as colposcopy with biopsy. A high percentage of colposcopies in comparison to the number of biopsies is a problem that demands an urgent solution [12]. It is however not yet certain what steps should be taken to provide proper and high-quality preventive measures in case of glandular premalignant cervical disease detection and also how to have open access to the use the HPV test as an effective tool in the diagnostics of cervical cancer [13-15].

From the results of our analysis, it may be concluded that improvements are urgently needed in Slovenia in the

field of screening for and early detection of cervical cancer [17]. It is first and foremost important,

– to continue with data gathering and analyzing the procedures performed in patients who were regularly attending a gynecologist before they were diagnosed with cervical cancer;

– to analyze individual cases, including independently reevaluating cervical smear samples or other pathohistological samples collected in the period within five years before the diagnosis of cervical cancer;

– to determine, similarly to organized screening programs for cervical cancer in other countries, the dates of refresher courses on colposcopy and time interval between two courses intended for all who are regularly performing colposcopy in order to improve the quality of performance of this procedure and of cervical smear collection, and to pay greater attention to the drawbacks observed in the follow-up findings of cervical cancer patients;

– to consistently urge following the recommendations for detecting, treating, and following-up patients with premalignant cervical disease;

– to facilitate as soon as possible systemic application of a HPV test as an additional diagnostic procedure in women with initial stage pathologic changes of a cervical smear and in those who were treated for CIN;

– to redirect a part of the activities of the departments of gynecology and obstetrics in Slovenian hospitals into more effective colposcopy clinics, which should be able to provide high-quality diagnostics, and fast and effective treatment of premaligant cervical disease in line with national guidelines imposing also the follow-up of quality indicators;

– to urge women to perform gynecological examinations regularly particularly in cases of pathologic changes of a cervical smear and other gynecological disorders associated with premalignant cervical diseases, as well as in women treated for CIN.

Acknowledgement

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