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# The value of gynecological cancer follow-up: a 15-year single institutional experience

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**Summary**

*Purpose of Investigation:* A routine follow-up is standard medical practice in patients treated for gynecological cancer. The aim of this study was to compare the survival differences between asymptomatic and symptomatic patients at the time of relapse. *Materials and Methods:* Retrospective cohort analysis. *Results:* All women diagnosed and treated for vulvar (n=78), cervical (n=289), endometrial (n=453), and ovarian cancer (n=261) between 2001 and 2015 were included in this study. The median survival time after recurrence between symptomatic and asymptomatic patients was in vulvar cancer (27 *vs.* 22 months, $p = 0.181$), in cervical cancer (10 *vs.* 13 months, $p = 0.123$), in endometrial cancer (19 *vs.* 30 months, $p = 0.265$) and in ovarian cancer (19 *vs.* 18 months, $p = 0.861$). *Conclusions:* There was no survival difference between asymptomatic and symptomatic patients at the time of relapse. Follow-up may become effective if the procedures are adapted to other aims of routine practice (e.g. psychosocial care and monitoring adverse effects of treatment).

*Key words:* Follow-up; Survival; Cancer; Endometrial; Ovarian; Cervical; Vulvar; Recurrence.

## Introduction

Traditionally, patients who have been treated for gynecological cancer undergo follow-up in secondary care. Cancer patients are living longer after or with gynecological malignancy. The main reason for routine follow-up is the detection of recurrent cancer before symptoms appear, earlier treatment, and improved survival rates. Routine follow-up after primary treatment has two objectives: 1) to detect complications related to treatment and 2) to detect recurrence earlier in order to improve the survival of patients with recurrent disease. Follow-up is based on periodic visits and examination combined with various tests for detection of treatable recurrent disease.

In Slovakia, no national guidelines on the follow-up of gynecological cancer patients have yet been published. This is mainly because the procedures are similar to those conducted in other European countries. However, in some published guidelines, the lack of evidence-based knowledge is reflected in the variations in recommended follow-up strategies [1-6]. In the present institute, cancer patients are usually followed-up every three months in the first and second year, every six months in the third to fifth year, and annually thereafter. Despite the follow-up, many recurrences are diagnosed in the interval between routine follow-up visits. Many patients, even when undergoing recurrent symptoms, have a tendency to wait for the next visit in the follow-up program. This of course might aggravate the symptoms, since examination is delayed. There is lack of consensus on effective strategies to address the need and length of follow-up.

The aim of this study is to compare the survival differences between asymptomatic and symptomatic patients at the time of relapse in Slovakian cancer patients in an oncogynecology center.

## Materials and Methods

The authors retrospectively reviewed all patients with vulvar, cervical, endometrial, and ovarian cancer, treated in the present institute from January 2001 through December 2015. The medical records were reviewed according to a computerized medical system and the following factors were obtained: age at the time of diagnosis, surgical procedure, histology, FIGO stage, grade, radiation therapy, chemotherapy, hormonal therapy, and follow-up status, which included the disease-free interval (DFI), overall follow-up, and survival after diagnosis of recurrence.

Inclusion criteria for patients in the study were the recurrence of disease, histological type (squamous cell carcinoma of the vulva, squamous cell and adenocarcinoma of the cervix, adenocarcinoma of the uterus, and epithelian ovarian cancer). Recurrence was defined as the reappearance of cancer ≥ 6 months after the end of treatment. Relapse, on the other hand, was identified if there was a recurrence after complete remission of the disease. Each of the symptoms was reviewed.

The authors defined complete remission as a status where there was no longer any presence of symptoms, gynecological and oncological examinations were negative, imaging methods had not shown any tumor, and tumor markers were negative (CA-125 < 35 IU/ml, SCCA < 2.2 ng/ml). Recurrence of disease was defined as the appearance of disease symptoms or asymptomatic conditions, and if relapse was demonstrated in one of the clinical examinations, imaging techniques (ultrasound, X-ray, CT, MRI, and

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PET/CT) or elevated levels of tumor markers. CA-125 elevation was considered positive when it was twice the value of its normal serum levels.

Exclusion criteria were: disease relapse within six months after stopping treatment and a patient relapsed at the end of the study in any type of sarcoma. All recurrences were cytologically or histologically verified.

Patients were divided into groups according to the type of the primary tumor and then each group into two subgroups according to the presence or absence of disease symptoms on an asymptomatic and symptomatic basis. Staging was determined according to the FIGO [7, 8].

Disease-free intervals were measured from the end of primary treatment to the date of recurrence (the first symptom or positive sign of examination or lab tests). Overall survival was measured from the time of surgery or primary radiotherapy to the date of death.

After primary treatment for ovarian, endometrial or cervical cancer, the authors arranged visits every three months for the first two years and every six months in years 3, 4, and 5. From six years after primary treatment, the authors conducted examinations annually. Each visit included the patient's history and a physical/gynecological examination, including abdominal and vaginal ultrasound, and a Pap smear. Examinations were carried out by gynecologists and clinical oncologists. Standard tests of patients with ovarian cancer were monitored for serum CA-125 or another tumor marker (CEA, CA72-4) in the case of an increased parameter value before primary treatment. The examination of patients after primary treatment for carcinoma of the cervix was carried out to determine the level of SCCA annually and chest X-rays were also performed. The examination of patients after primary treatment for endometrial cancer included the a chest X-ray once a year. Examination of the levels of CA-125 was not part of the routine check up. After primary treatment for carcinoma of the vulva, the oncogynecologist performed check ups on patients every three months during the first three years and subsequently every six months. All visits involved the measurement of SCCA serum levels.

The history of the primary treatment of examined patients: in the case of vulvar cancer it included radical vulvectomy or hemivulvectomy (1 cm margin) with inguinal lymphadenectomy, and as for cervical cancer, it included abdominal radical hysterectomy (nerve-sparing technique) with pelvic lymphadenectomy. In the case of endometrial adenocarinoma, it included total abdominal hysterectomy and bilateral salpingo-oophorectomy (pelvic and para-aortic lymphadenectomy which were performed in high-risk patients). Surgical staging was the usual procedure for ovarian cancer, which included total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymphadenectomy, appendectomy, peritoneal cytologic examination, and/or primary cytoreductive surgery for advanced ovarian cancer. Radiotherapy of vulvar cancer was individualized based on the clinical circumstances. Daily fraction were generally 1.8 Gy to a dose 45-54 Gy in the absence of gross disease, positive margins 54 Gy, and gross disease generally 60 Gy. The cervical cancer patients (Stages IB an IA) with high-risk pathologic factors (e.g. positive lymphatic nodes) underwent adjuvant radiation therapy with concurrent cisplatin-based chemotherapy 40-50 Gy. The endometrial cancer high-risk patients underwent postoperative radiotherapy 45-50 Gy. Cytoreductive surgery followed by paclitaxel/platinum-based chemotherapy was standard treatment of advanced ovarian cancer (six courses).

Survival curves were calculated using the Kaplan-Meier method. Medians (the disease-free interval and survival after detection of recurrence) were compared using the Wilcoxon-Rank test. These were used to determine significant differences wherever found ($p < 0.05$). All statistical analysis were performed using SPSS ver. 20.0. Informed consent was obtained from participants in the study and the institution's ethics committee approved the study.

## Results

Clinical characteristics of the study participants with recurrence are reported in Table 1. Seventy-eight patients with vulvar cancer underwent primary treatment. Twenty-eight (47.4%) patients had recurrent disease. The DFI was 16 (range 8-44) months. The median DFI of asymptomatic patients was 22.5 (range 10-41) months and the median DFI of symptomatic patients was 14.5 (range 8-44) months. There was no significant difference in the DFI of asymptomatic and symptomatic patients ($p = 0.126$).

The median survival after detection of recurrence in asymptomatic patients was 22 (range 15-48) months and in symptomatic patients 27 (range 6-36) months. Three patients died six months after diagnosis of recurrence; 25 of 28 (89.2%) patients lived more than 12 months after diagnosis of recurrence; 15 of 28 (53.5%) patients lived for more than 24 months, and 25 of 28 (89.2%) patients died before the end of three years after diagnosis of recurrence. There were no statistically significant differences between patients with asymptomatic and symptomatic recurrences ($p = 0.181$, Figure 1).

Two hundred eighty-nine patients with cervical cancer underwent primary treatment and 62 (28.7%) patients had recurrent disease after the end of treatment. The number of patients with residual disease was 35 of the 202 (17.3%) who underwent primary surgical treatment and 25 of the 87 (28.7%) who underwent primary radiation therapy. The median DFI was 15 (range 7-40) months, with the median DFI of asymptomatic patients at 12 (range 8-26) months and the median DFI of symptomatic patients at 11 (range 7-40) months. The median DFI of patients with local recurrences was 11 (range 7-26) months and patients with distant recurrences was 24 (range 10-40) months. There was no significant difference in the DFI of asymptomatic and symptomatic patients ($p = 0.173$).

The median survival of patients with asymptomatic recurrences was 12 (range 7-20) months and for patients with symptomatic recurrences ten (range 2-30) months. Fifty-two (83.8%) patients with recurrences were alive after six months, 45 (72.5%) patients were alive after one year, and three (4.8%) patients were alive after two years. In 16 (25.8%) patients with asymptomatic recurrences, recurrent disease was discovered at the time of the routine follow-up consultation, while 36 of 46 (78.2%) symptomatic patients had interval recurrences. There were no statistically significant differences between patients with asymptomatic and symptomatic recurrences ($p = 0.123$, Figure 2).

During the study period, 452 patients with endometrial

cancer underwent primary treatment; 73 (23.4%) patients had recurrent disease. The median DFI was 15 (range 7-48) months. The median DFI of asymptomatic patients was 23 (range 7-48) months, and the median DFI of symptomatic patients was 14 (range 7-36) months. There were no significant differences in the DFI of asymptomatic and symptomatic patients ($p = 0.092$). The median survival after detection of recurrence of patients with asymptomatic recurrences was 30 (range 7-62) months. For patients with symptomatic recurrences, it was 19 (range 7-108) months. Sixty-five of 73 (89%) patients were alive six months after diagnosis of recurrence; 26 of 73 (35.6%) patients were alive after two years, and 11 of 73 (15%) patients were alive after three years. Among patients with recurrence, there were no differences in the overall survival rates between patients with asymptomatic and those with symptomatic recurrences ($p = 0.265$, Figure 3).

Two hundred sixty-one patients with epithelial ovarian cancer underwent primary surgical treatment, and 84 (49.1%) patients had recurrent disease after the end of treatment. The median DFI was 14 (range 6-33) months. The median DFI of symptomatic patients was 14 (range 6-27) months, and the DFI of asymptomatic patients was 13 (range 6-33) months. There was no significant difference in the DFI of asymptomatic and symptomatic patients ($p = 0.855$). The median of survival after detection of recurrence of patients with asymptomatic recurrences was 18 (range 6-42) months and of patients with symptomatic recurrences was 19 (range 6-39) months. Seventy-nine (94%) of 84 patients were alive after six months, 68 (80.9%) of 84 patients were alive after 12 months, and 18 (21.4%) of 84 patients were alive two years after diagnosis of recurrence. There were no statistically significant differences in overall survival between patients with asymptomatic and symptomatic recurrences ($p = 0.861$, Figure 4).

## Discussion

The data presented in the present article show that there was no statistical difference in survival rates between the group with recurrences detected during a routine follow-up and those with recurrences that were detected when the patients developed symptoms. The main limitation of this study is a retrospective analysis, which suffers from incomplete data collection and is subject to allocation and exclusion bias, as well as length-time and lead-time biases. The authors recognize that the length-time bias can only be eliminated by a prospective analysis. A randomized design is the only valid approach to achieve an unconfounded estimate of the effectiveness of follow-up programs. Obtaining a sufficient number of patients for the purpose of this type of study can create problem. Essentially all patients prefer to undergo conventional follow-up program. They believe that early detection of relapses leads to prolonged or to saving their lives. Ethical assessment of this fact can be complicated.

The number of oncogynecologists in Slovakia is limited, as well as abroad. The existing follow-up program leads to an increased work-load of specialists and may lead to a decreased quality of care. On the other hand, quality control of specialists' own work, detection of sequelae after treatment, and credit and appraisal from the patients are important benefits for doctors [9]. For low-risk cancer patients, follow-up in primary compared to secondary care is of interest, as recurrences are rare and it would decrease the workload of the hospital specialists [1]. As many as 47% of the experts considered less intensive follow-up for low-risk patients to be adequate, although gynecological oncologists in low economy countries are more conservative and preferred traditional follow-up [10].

Existing follow-up program brings comfort to the patients. The first visit is important. Patients know they belong somewhere and have planned appointments. The follow-up program seems to bring the patients security and comfort; sometimes on the other hand may induce depression/anxiety and dubiousness. It is correct to completely inform the patient. However, specialist cannot permit patients to lose hope.

Prognosis of the cancer is changing, mainly due to new inventions in the fields of genetics and chemotherapy. Patients have to be an integral part of therapeutic team and should be a "specialist" when it comes to their illness.

According to the present data, the authors cannot expect intensive follow-up procedures to be better than surveillance on demand. As the optimal follow-up schedule is unknown, the authors cannot define the optimal follow-up program because gynecology cancer patients are very different, depending on initial therapeutic procedures.

The recurrences of vulvar cancer in the present series were 35.8%; local recurrences were 50%, inguinal 35.7%, and distant 14.2%. A similar count of local recurrences was indicated in the findings of Cheng *et al.* and Maggino *et al.*, although the number of inguinal recurrences in the present study is two-fold, respectively, compared with the mentioned studies [11,12]. According to Chang *et al.* the five- and ten-year disease-free survival rates were 66.5% and 45.2%, respectively [12]. Rhodes *et al.* as well as Woolderink *et al.* found the recurrence rate of cancer of the vulva to be 30% and 35%, respectively [13, 14]. The Woolderink *et al.* study reported a 23% incidence of local recurrence, a 9% incidence of inguinal recurrences, and a 3% incidence of distant recurrences; after a local recurrence, 72% of patients developed a second local recurrence. These patients are at high risk and require a close follow-up [13]. The present results are very similar, although the authors followed four-times fewer the number of patients. There were no "bridge" metastases.

Nordin *et al.* indicated that the routine monitoring of patients after primary treatment for vulvar cancer in the early stages is not effective, and that patient education, with

Table 1. — *Characteristics of symptomatic and asymptomatic patients with recurrence (DFI-disease free interval, SAR-survival after recurrence).*

| Characteristics | Vulvar cancer | Cervical cancer | Endometrial cancer | Ovarian cancer |
|---|---|---|---|---|
| Number of patients with recurrence | 28 (47.4%) | 62 (28.7%) | 73 (23.4%) | 84 (49.1%) |
| Age, years (range) | 69 (31-63) | 44 (31-63) | 62 (40-83) | 52 (30-76) |
| Asymptomatic | 11 (39.2%) | 16 (25.8%) | 19 (26%) | 50 (59.5%) |
| Symptomatic | 17 (60.7%) | 46 (74.1%) | 54 (73.9%) | 34 (40.4%) |
| FIGO Stage | | | | |
| I | 5 | 20 | 35 | 5 |
| II | 16 | 31 | 21 | 8 |
| III | 6 | 11 | 13 | 71 |
| IV | 1 | 0 | 4 | 0 |
| Location of recurrence (n) | | | | |
| Inguinal nodes | 10 | | 4 | 2 |
| Vulva | 14 | | | |
| Chest | 2 | 14 | 9 | 6 |
| Bone/skeleton | 2 | 5 | 16 | |
| Pelvis | | 23 | 7 | 32 |
| Pelvic nodes | | 5 | | |
| Vagina | | 5 | 7 | |
| Brain | | | 2 | |
| Liver+nodes | | 3 | 3 | 15 |
| Retroperitoneal nodes | | 4 | | 14 |
| Peritoneum | | 3 | 25 | 15 |
| Symptoms (n) | | | | |
| Bleeding | 1 | 5 | 7 | |
| Pain | 9 | 29 | 38 | 23 |
| Vulvar itching | 5 | | | |
| Inflammation | 2 | | | |
| Cough | | 4 | 5 | 3 |
| Hemoptysis | | 2 | | |
| Ileus | | 4 | | 6 |
| Anaemia | | 1 | | |
| Pain+bleeding | | 1 | | |
| Dyspnea | | | 3 | |
| Neurological changes | | | 1 | |
| Icterus | | | | 2 |
| Median DFI (months) | | | | |
| Asymptomatic (range) | 22.5 (10-41) | 12 (8-26) | 23 (7-48) | 13 (6-33) |
| Symptomatic (range) | 14.5 (8-44) | 15 (7-40) | 14 (7-36) | 14 (6-27) |
| *p* | 0.126 N.S. | 0.173 N.S. | 0.092 N.S. | 0.855 N.S. |
| Median SAR (months) | | | | |
| Asymptomatic (range) | 22 (15-48) | 13 (7-20) | 30 (7-62) | 18 (3-42) |
| Symptomatic (range) | 27 (6-36) | 10 (2-30) | 19 (3-108) | 19 (6-39) |
| *p* | 0.181 N.S. | 0.123 N.S. | 0.265 N.S. | 0.861 N.S. |

symptom-triggered rapid clinic access, may be more effective [15]. However, a comparison with the present patients is not appropriate due to many variable factors. In this case, they are followed up by a gynecologist or oncogynecologist. At the same time, there is free access to a specialist in case any specific medical attention is needed. The frequency of follow-up in this study is higher than those mentioned in the aforementioned studies, with asymptomatic patients representing 39.2%. Shorter interval checks were found to be a major factor in early detection of relapse. However, any inference that this prolongs survival is questionable.

Maggino *et al.* pointed out that a 25% local recurrence was detected after four years from the completion of primary treatment [11]. Further work indicated that about 50% of local recurrence occurs between the second and third year of follow-up [16, 17]. In the present series, the median DFI of local recurrence was 18.5 months. Despite several published articles on this topic, it is unclear whether early detection of asymptomatic recurrence prolongs survival. The reasoning of Maggino *et al.* is mainly limited by the possibility of therapy for metastatic disease. This is also the reason why imaging is indicated only in cases of symptomatic recurrences [11].

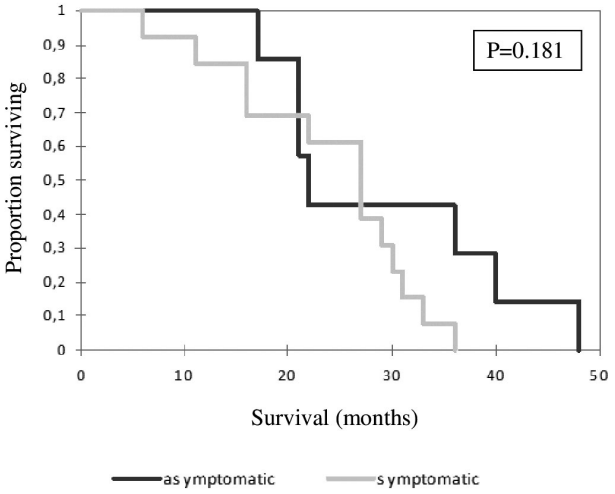


Figure 1. — Kaplan-Meier curves showing survival of patients with vulvar cancer after detection of recurrence.

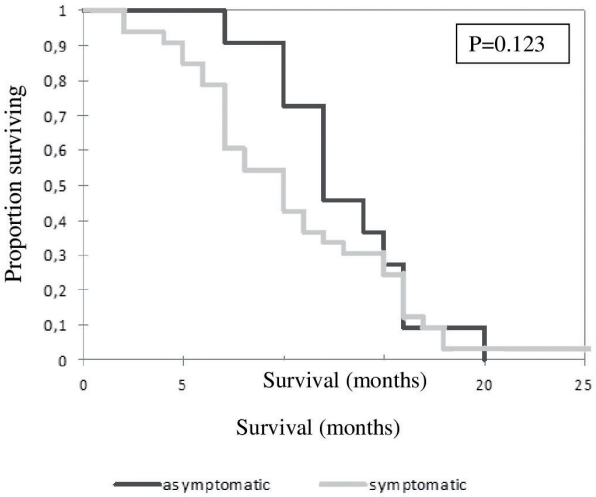


Figure 2. — Kaplan-Meier curves showing survival of patients with cervical cancer after detection of recurrence.

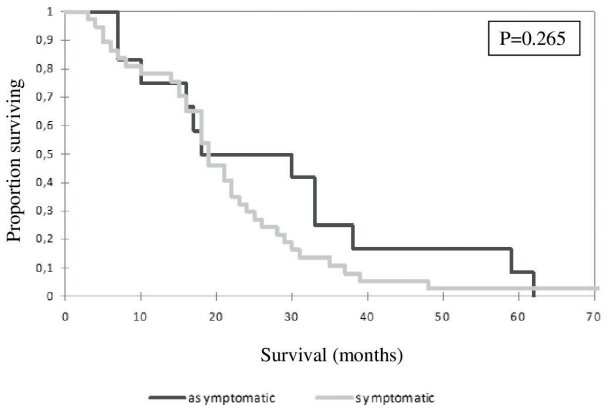


Figure 3. — Kaplan-Meier curves showing survival of patients with endometrial cancer after detection of recurrence.

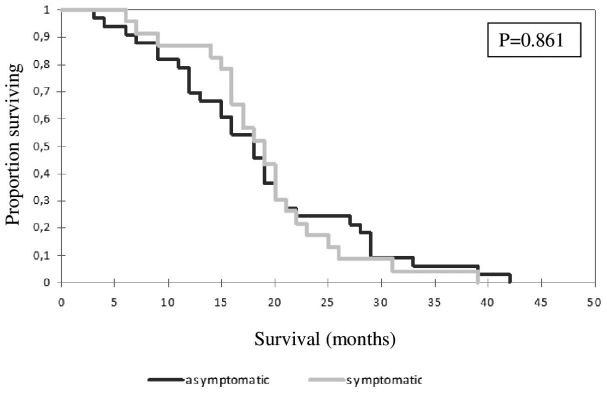


Figure 4. — Kaplan-Meier curves showing survival of patients with ovarian cancer after detection of recurrence.

The group of patients with carcinoma of the vulva consists of specific older age patients with a co-morbidity and typically requires an open approach to consultation. Overseeing and guidance that can be provided for this group will mainly focus on psychological support, detection and management of complications of treatment. It may also assist in data collection for the purpose of further studies.

The value of the results of studies on recurrence of the vulva is limited to a relatively small number of patients in the files. Given the age and comorbidity of the patients, it is complicated to impact the assessment of underlying disease on the survival of patients.

Recurrence of cervical cancer in the present group was found in 21.4% cases. Monk *et al.* indicate that one in three patients with invasive cervical cancer progresses to tumor relapse [18]. According to Morice e*t al.* follow-up of patients treated for cervical cancer based on routine Pap smears and systematic radiography does not permit earlier detection of recurrence and does not increase survival [19]. The relative incidence of relapses in the various studies referred to is in the range of 13-17%, while the majority of these patients are in Stage I and II of the disease according to FIGO [19-22]. The results of these works indicate that while the incidence of relapse in Stage IB-IIA is 10% to 20% in the lymph nodes, it increases at a later stage to a value of 70%, respectively [21-24].

The present results confirm the assumption that most patients at the time of recurrence of cervical cancer are symptomatic. Similar results were also published by Bodurka-Bevers *et al.* [20]. Duyn *et al.* found that the abundance ratio of recurrence is 45% for patients in the entire group, recurrence was detected during a scheduled follow-

up visit in only 32% of all cases. In recurrent disease, the DFI was a prognostic factor for survival [21].

Bodurka-Bevers *et al.* indicated that post-therapy surveillance programs are directed towards asymptomatic patients in whom early detection of recurrence may impact survival, and data from their study indicate that a subset of women may benefit from such surveillance [20]. According to Ansink *et al.* routine follow-up surveillance is ineffective in detecting recurrent cervical carcinoma [22].

The incidence of the interval of recurrence in the present series was 57%, respectively, while Zola *et al.* found 29.7% [25]. One reason for the higher number of relapses diagnosed in these patients might be the good education of the patients themselves, while on the other hand, a higher incidence of recurrence of aggressive types of carcinoma that produce symptoms in a short period of time could be another cause.

While there is a large number of asymptomatic patients, in small studies, only one of these studies reported that detecting asymptomatic recurrence is associated with longer overall survival as well as with longer survival following the detection of recurrence in patients in comparison with those with a symptomatic relapse. The probable cause was indolent ongoing relapse [25]. Mabuchi *et al.* showed that the patients who were first diagnosed with abnormal physical findings (Pap smear, CT scan) had a significantly better survival rate than those who first presented with symptoms. This indicates that patients may benefit from a routine follow-up using these diagnostic procedures for detecting asymptomatic recurrence [26].

Zola *et al.* published a study in which and they found that only 50.1% of patients had asymptomatic recurrence of cervical cancer [25]. Ansink *et al.* found 13% representation of patients with asymptomatic recurrence, Bodurka-Bevers *et al*. 14% and Duyn *et al.* 13% [20-22]. The numbers of patients with asymptomatic recurrences represented 25.8% in our series.

The present authors observed 37.1% of recurrences in the pelvis, 54.8% as distant recurrences, and in 8.1% of patients had a combination of distant and local recurrence. Zola *et al.* reported a 71.6% incidence of local recurrence, 24.2% distant recurrence, and 4.3% distant and local recurrence combined [25]. Bodurka-Bevers *et al.* ascertained that 37 patients recurred in the central pelvis, 21 each in the lung or pelvic wall, 22 in nodes, and 35 in other sites. The data in the study by FIGO Stage IB was obtained only from recurrence after radical treatment [20].

In the present groups of patients, there were no statistically significant differences in the survival rates between the two groups. Similar conclusions have also been published by other authors [19-22]. Only one retrospective analysis, published by Zola *et al.*, found a statistically significant difference in survival for patients with asymptomatic recurrence of the disease, although the authors considered it necessary to verify these findings in a prospective study [25].

In patients with endometrial cancer, it has not been proven whether follow-up is associated with survival benefits. Accordingly, in the present study there were no statistically significant differences in the survival of patients after detection of disease recurrence.

Reddoch *et al.* found a 11% recurrence rate, where 41% of patients were symptomatic and 59% were asymptomatic. According to these authors, further investigation methods would increase the cost of tracking with no positive impact on survival, as 56%-70% of recurrences were apparently detected in a basic gynecological examination [27].

Berchuck *et al.* showed a 12% incidence of recurrence. During a ten-year period in which 510 patients were followed, 44 cases of localized recurrence were estimated in the following locations: 27% vagina and cervix, 27% pelvis or vagina and abdominal cavity, 10% lungs, 29% pelvis/abdominal cavity and distant recurrence, and others 7%. According to this study, the low recurrence rate of FIGO Stages I/II endometrial cancer and the paucity of effective second-line treatment, surveillance Pap smears and chest radiographs appear to have little impact on survival [28]. In the present study, the authors found a different localization of recurrences, probably because they processed a set of patients in all stages by FIGO and not just those in Stages I and II. The authors indicated that the monitoring was associated with a large number of examinations in order to detect potentially curable five asymptomatic recurrences. Overall survival in the whole group was only 1.2%. This generally indicates that in the case of detection of recurrence of endometrial cancer, the subsequent treatment is successful in only 10-20 % of patients [28]. In the present series, the authors found seven asymptomatic recurrences in the vagina. One patient died after seven months and the other after 33 months.

Owen and Duncan published a study in which they found 16.6% recurrences of endometrial cancer. Of the 17 patients with the relapsed disease, 79% were symptomatic at the time of the recurrence. There were no statistically significant differences in survival between symptomatic and asymptomatic patients [29]. Several patients in the present study had longer survival. Comparison of survival is problematic, however, which were discovered because in this study the authors worked with a four-fold greater number of patients.

Salvesen *et al.* indicated a 18.8% incidence of recurrence of endometrial cancer. In low-risk patients in Stages IA and IB according to FIGO, they did not even find one asymptomatic recurrence, and low risk women should be considered for an alternative, less frequent follow-up. The high-risk group required 653 regular examinations to detect one asymptomatic recurrence [30].

Agboola *et al.* found 11.57% recurrences and stated that there was no statistically significant difference in the survival of patients with symptomatic and asymptomatic re-

currence of endometrial cancer. Intensive monitoring does not improve survival of patients, although it may contribute to reducing morbidity and improving quality of life [31].

Shumsky *et al.* conducted a study similar to the present range, which followed 317 patients after primary treatment and found 53 patients with relapsed disease (16.7%), 75% of whom were symptomatic. Seventy percent of the recurrences were detected within the first three years of follow up. There were no statistically significant differences in the survival rates of patients with symptoms of the disease and patients whose relapse was detected during a routine examination [32]. The results of this study are almost identical with the results of the present study.

Tjalma *et al.* found a 13% recurrence rate, 83% of which were symptomatic. The discussion concluded that regardless of the presence or absence of symptoms of recurrence, the survival of patients is different [33].

Lajer *et al.* indicated that during the first three years after primary treatment, they found a 70-95% recurrence of endometrial cancer. The relative incidence of recurrence is 8%-19% [34]. The risk of recurrence in the "low-risk" group is from 1%-3%, and the risk of recurrence in the "high-risk" group is from 5%-16%. The representation of relapses in both of these risk groups nearly doubled in the present study. The reason was probably due to the classification of patients into risk groups, with different working groups subjected to different criteria [27, 28, 31, 35-37].

Gadducci *et al.* reported that an intensive surveillance protocol seems to have no significant impact on the outcome of patients in Stage I endometrial cancer. Simplified follow-up programs tailored for patient subsets with different recurrence risk are required [35].

Fung-Kee-Fung *et al.* evaluated the benefit-risk monitoring for both groups of patients. Only two out of 1,000 patients from low-risk groups show at benefit from follow-up. On the other hand, only seven out of 1,000 patients from high-risk groups benefit from early detection of disease recurrence. Given the percentage of high-risk groups and the number of relapses, it is necessary to perform a large number of tests to detect a small number of recurrences in the low risk group. Counseling on the potential symptoms of recurrence is extremely important because the majority of patients with recurrences were symptomatic [38]. Carrara *et al.* showed that women with asymptomatic recurrence showed a better clinical outcome compared with those with symptomatic relapse [39].

The present authors analyzed the survival of patients after primary treatment for ovarian cancer and found recurrence in 32.1% of cases. In the early stages of the disease (Stages IA-IIA according to FIGO), the authors found recurrence in 19% and in the advanced stages (Stages IIB-IV according to FIGO), and recurrence in 67% of patients. Gadducci *et al.* presented the abundance ratio in the early stages of recurrence at 20%-30%, and in the advanced stages at 50%-75%, while Czech authors reported the risk of recurrence in the early stages at 10%-20% and in advanced stages at 60%-85% [40, 41].

Gadducci *et al.* observed that the presence of symptoms at the time was found to be a prognostically irrelevant factor. In conclusion, there are were differenced in the survival of patients with symptomatic and asymptomatic recurrence of ovarian cancer [42].

Chan *et al.* assessed different methods of follow-up, and 45% of patients had asymptomatic recurrence and 55% symptomatic recurrence of the disease. There were no statistically significant differences in the survival of these two groups of patients, questioning the role of routine surveillance of patients. Routine physical examination had a very limited additional role and could be possibly omitted as part of the routine follow-up strategy [43]. In the present study the authors found equally distinct survival rates in these two groups of patients.

Tanner *et al.* formed an exception and showed improved survival duration in patients with their recurrence detected in the asymptomatic phase as compared with patients with a symptomatic recurrence. This difference can be explained by the length-time bias [44]. The results of the mentioned study are in contrast to those observed in the present work.

Geurts e*t al.* published their paper in 2012 and concluded that routine follow-up in ovarian cancer patients is not expected to improve life expectancy. The timing of detection of recurrent ovarian cancer is immaterial until markedly improved treatment options become available [45].

Patients with relapsed ovarian cancer have a very poor prognosis. Median overall survival is less than two years and the five-year overall survival rate is less than 10% [46, 47]. Von Georgi *et al.* indicated in their study that there was no evidence of intensive follow-up offering higher chances of survival. However, more intensive surveillance after a period of two years may have proven beneficial [47]. Recurrence of the disease for most patients is infaust. Geurts *et al.* examined the effectiveness of monitoring and found that five published studies did not confirm the assumption of a positive impact of monitoring on survival [46].

Rustin *et al.* in a study of early treatment of relapse of the disease on the basis of CA-125 elevation, emphasized that long treatment period reduced quality of life caused by the long treatment period [48]. In both studies it was predicted that no impact on survival would be observed in patients who were not monitored at all. This was because such a practice of not following up is considered to be unethical [49].

The regular monitoring of serum levels of CA-125 is associated with a reduction in the quality of life. It is usually possible that with an indication of elevation, the programming of other therapeutic procedures can be conducted [48]. Monitoring of CA-125 should be carried out according to published recommendations [50].

A potential source of problems are patients for whom effective treatment is not actually available. Early detection

of recurrence may lead to changing the patient's quality of life. In ovarian cancer for instance, the median lead time between elevated CA-125 levels and clinical evidence of recurrence is three to five months [49]. The question is whether anxiety or stress is an acceptable compromise for a follow-up.

## Conclusions

The results of the present study are a reflection of single institution oncological care in a certain time period. Since so far there is no clear evidence of the positive impact of surveillance on patient survival, it is necessary to focus on other aspects of care, particularly to improve the quality of life of patients. Survival of patients depends primarily on the perfect primary therapy, especially surgical treatment. Personalised treatment, individual approach with psychosocial support, and treatment of side-effects are key modes for better quality of the life. It is time for a new model of follow-up with focus on quality of life, quality of care, and patients' needs.

A follow-up program does not have an effect on the prognosis of cancer. The optimal approach is unknown and randomized controlled trials comparing follow-up protocols are still missing. Regular routine follow-up visits and technical examinations carry a financial burden. They cannot be justified if there is no benefit. It is necessary to review the time and money which is spent on healthcare, especially in the follow-up program and we have to concentrate only on efficient activity. Quality of life of cancer patients is expressed between the measurable values of treatment and patient's condition, which is expressed by their hopes and expectations.

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