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**POPESCU ALIN**

# PhD THESIS

## “OUTCOMES OF CERVICAL CANCER MANAGEMENT BEFORE AND DURING THE COVID-19 PANDEMIC”

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# CHAPTER 1. COVID-19 PANDEMIC EFFECTS ON CERVICAL CANCER DIAGNOSIS AND MANAGEMENT: A POPULATION-BASED STUDY IN ROMANIA

## BACKGROUND

As a preventative step against SARS-CoV-2 infection, the Romanian government took the same precautions as other nations within the European Union and placed a temporary pause on the nation's screening programs during the lockdown that occurred at the peak of the pandemic. Women between the ages of 21 and 65 were eligible to get free yearly Pap smear tests as part of this program. These tests are used for the screening and early diagnosis of cervical abnormalities. We have observed a significant decrease in the number of newly diagnosed cases of cervical cancer, as well as a decrease in the number of women requesting investigations for cervical cancer in our clinical practice during the past 24 months of the ongoing pandemic, despite the fact that official statistics regarding the cases of cancer diagnosed during the COVID-19 pandemic have not yet been released. This is despite the fact that there is still an ongoing pandemic. Concerns were raised as a result over the total number of cervical cancer cases that had been overlooked. In light of this hypothesis, we devised a research project with the objective of determining the impact that the first 24 months of the COVID-19 pandemic had on the distribution of cervical cancer tests, the stage at which newly diagnosed patients with cervical cancer were found, and the patients' access to cancer treatment.

The evaluation took into account a number of different variables, including patient background information; the number of cervical cytology tests, HPV tests, and colposcopies performed; tumor staging; the amount of time that passed between the biopsy and the first visit to the cancer center; and cancer treatment between the pre-pandemic and pandemic periods. The staging of cervical cancer according to the 2018 guidelines established by the International Federation of Gynecology and Obstetrics (FIGO) staging method. It was determined that the 24 months beginning in January 2018 and ending in January 2020 constituted the pre-pandemic period, whereas the years beginning in January 2020 and ending in January 2022 were regarded to be the pandemic period.

The patient loss ratio, abbreviated as PLR, was calculated to provide subpopulation-specific comparative metrics of change in the number of patients who presented themselves for cervical cancer examinations. The pandemic loss rate (PLR) was calculated by dividing the difference between the pre-pandemic yearly average by subpopulation (PP) and the during-pandemic yearly number of patients by subpopulation (DP) by the monthly average during the pandemic. The PLR formula is: PLR = (PP-DP)/MA. This formula was derived by dividing the difference between the pre-pandemic yearly average by subpopulation (PP) and the during-pande (MA). When the PLR levels are positive, this suggests a decrease in investigations, however when the PLR values are negative, this suggests an increase. The

magnitude of the PLR value provides an indication of the proportional degree to which the inquiry has shrunk or grown.

## RESULTS

Since the beginning of the COVID-19 pandemic in Romania in February 2020, and the subsequent lockdown measures implemented to delay the spread of SARS-CoV-2, we have seen a significant decrease in the number of cervical cancer screening tests as well as newly diagnosed cases of cervical cancer patients. This is due to the fact that lockdown measures were implemented to delay the spread of SARS-CoV-2. Despite the lack of any cause to predict a sudden change in epidemiological trends, this reduction followed a pattern that was noticeably different from what had been seen in the prior two years (2018 and 2019). Therefore, the fundamental assumption that is supported by existing cancer burden data is that it typically takes between ten and twenty years for cervical cancer to develop. Because of this, the number of new cervical cancer cases did not naturally decrease or remained equivalent to the year before the start of the COVID-19 pandemic; however, fewer of these new cases were effectively identified throughout the follow-up period. Figure 1 provides a complete profile of the women who visited our outpatient clinic for study of cervical cancer before and during the COVID-19 pandemic.

A nearly linear increase in the number of cervical cancer screening tests was detected between 2018 and 2020, with minor seasonal fluctuations. This pattern was observed despite the fact that there were four more years of data to analyze. However, when the pandemic began in the beginning of 2020, we noticed a significant decline in the number of tests that were carried out. This decline ranged from a low of -17 percent and a high of -62% in the months of January and February, respectively, to a low of -75% in the months of April and May, when compared with the same months that occurred before the pandemic. Since that time, a modest but continuous upward tendency has persisted, despite the fact that there have been numerous months during which testing has been reduced. This is in line with the pandemic waves and government limits. The numbers managed to get back up to 36.1% of what they were during the same time period prior to the COVID-19 pandemic in the last month of 2021, although they were still much lower than what was previously regarded as normal. In general, investigations into cervical cancer were substantially impacted by a decline in the volume of tests that was equivalent to an average percent change of 49 percent throughout the two years that the pandemic was active (confidence interval [31.7; 68.6], p-value 0.001).

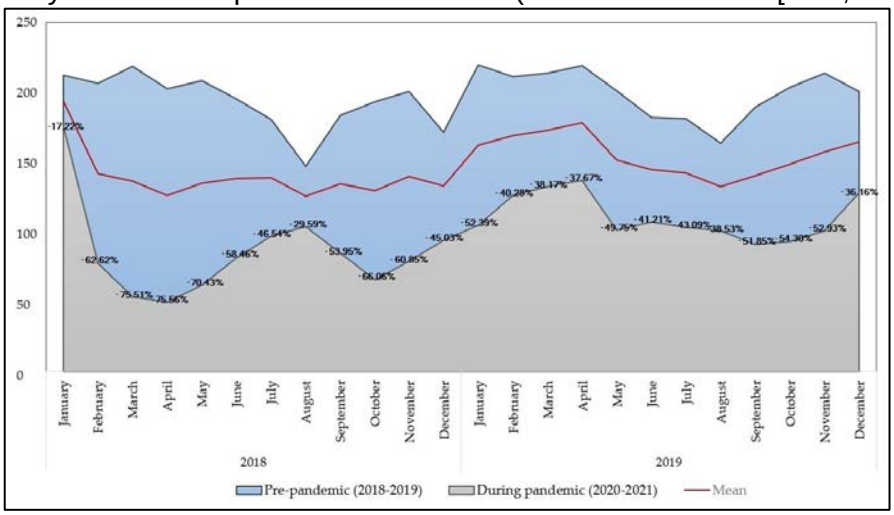

Figure 1. Evolution of cervical cancer screening before and during the COVID-19 pandemic.

When comparing the two time periods of the research, there was a statistically significant age gap when looking at both the average age of patients and the age groups they belonged to. The difference in mean age between before and during the pandemic was 33.6 years, with a value of 0.002 for the p-value. Before and during the pandemic, the majority of

patients who presented for investigations were in the age category of 21–35 years old (53.4 percent respectively, 56.8 percent, p-value = 0.003). The age group ranging from 50 to 65 years old had the highest patient loss ratio. Other significant findings were identified in the level of income. The majority of patients were in the medium income range prior to the pandemic (53.4 percent vs. 51.3 percent during the pandemic), with the lowest-income group experiencing the highest patient loss ratio (from 24.3 percent to 19.4 percent, p-value 0.001) during the pandemic. During the COVID-19 pandemic, there was a significant drop in the number of patients who were employed as well as those who were self-employed; however, the proportional loss of patients was greatest in the self-employed group (p-value 0.001) In conclusion, we found that the level of education of patients who requested cervical cancer investigations dropped by a statistically significant amount during the pandemic.

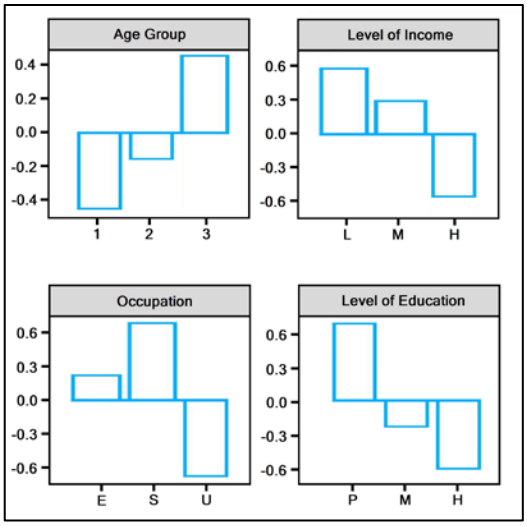


Figure 2. Patient loss ratio for cervical cancer investigations during the COVID-19 pandemic. Age Group: 1 – 21-35 years, 2 – 35-50 years, 3 – 50-65 years; Level of Income: L – Low, M – Medium, H – High; Occupation: E – Employed, S – Self-Employed, U – Unemployed; Level of Education: P – Primary, M – Middle, H – High.

The proportion of Pap smears, HPV tests, and colposcopies performed during the pandemic all contributed to a considerable drop in the overall number of individual testing for cervical cancer. During the pandemic, the proportion of people who had to wait more than four weeks for test results was statistically substantially greater (5.5 percent vs. 14.7 percent, p-value 0.001) than it had been prior to the pandemic. Since the beginning of the study, there has been a considerable reduction in the number of new cases of cervical cancer, with a decline of 45 percent (confidence interval [31.6; 53.3], p-value 0.001). Similar worrisome findings were found in the stage of cancers newly diagnosed, with a significant difference in stage III cancers of 21.4 percent more during the pandemic (p-value = 0.018). During the pandemic, there was an increase in the number of newly diagnosed cases of cancer. Last but not least, we found that patients who had recently been diagnosed with cervical cancer took a significantly longer amount of time to make it to their first visit to a cancer center (4.1 months vs. 6.4 months, p-value 0.001), and they missed significantly more appointments than they did during the pre-pandemic era (16.1 percent vs. 7.6 percent, p-value 0.002).

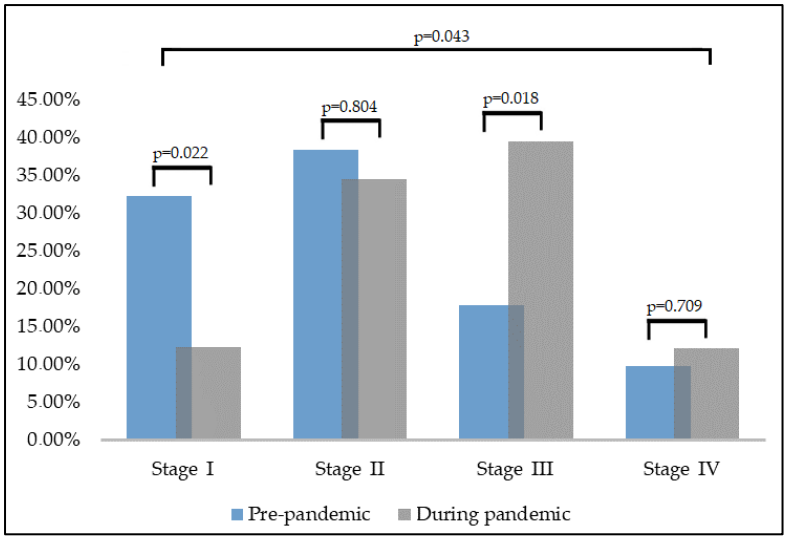

Figure 3. Screening outcomes for cervical cancer stages before and during the COVID-19 pandemic. The period reported as before pandemic spreads between 2018 and 2019, while the period during pandemic spreads between 2020 and 2021.

## CONCLUSIONS

The first twenty-four months of the COVID-19 pandemic witnessed a considerable decrease in the number of investigations done to identify cervical cancer. At the same time, however, an increase in the number of cervical cancer patients undergoing treatment was seen during this time period. There is still a significant gap that has the potential to result in the late detection of a big number of cases of cervical cancer. This gap exists despite the fact that the numbers are gradually growing. People who are newly diagnosed with the illness are frequently found to be in more advanced stages of the disease, and the pandemic circumstances make it more difficult to receive cancer treatment. In addition to the fact that we are failing to identify these instances, people who are newly diagnosed with the illness are often found to be in more advanced stages of the disease. We strongly encourage the introduction of additional strategies to bridge the diagnostic and treatment gap that exists between the pre-pandemic and post-pandemic periods of time for cervical cancer. This gap exists between the time when cervical cancer was not yet a pandemic and when it became a pandemic.

# CHAPTER 2. COVID-19 PANDEMIC IMPACT ON SURGICAL TREATMENT METHODS FOR EARLY-STAGE CERVICAL CANCER: A POPULATION-BASED STUDY IN ROMANIA

## BACKGROUND

In the majority of instances, curative treatment is able to be completed in the early stages of the problem, which is when it is indicated that surgical removal take place. The Wertheim–Meigs treatment, also known as radical hysterectomy with pelvic lymphadenectomy using an open surgical approach, is the conventional kind of operation that is used in these kinds of situations. The Wertheim–Meigs procedure was initially implemented more than a century ago, and while it has gone through some minor modifications over the course of time as a result of advancements in both surgical and medical practice, the procedure is essentially the same as it was when it was first used. One of the many minimally invasive operations that can now be performed thanks to the development of surgical robots is a robotic-assisted hysterectomy, which performs the same function as the Wertheim–Meigs method. The advent of surgical robots made it possible to perform a wide range of these procedures.

The treatment of a patient population that has cervical cancer at a more advanced stage demands various medicinal and surgical approaches. This, in turn, may have an

influence on the chance of morbidity and mortality within the patient population. In light of the numerous alterations and disruptions that occurred in the healthcare systems during the COVID-19 pandemic, we made the decision to carry out a study in order to determine the impact that the pandemic had on the surgical care that was provided to patients suffering from cervical cancer and to evaluate any changes in the management of these patients that may have an impact on their chances of survival. This study was carried out in order to determine the impact that the pandemic had on the surgical care that was provided to patients suffering from cervical cancer. The research was conducted over the course of a total of six years, beginning on January 1, 2016, and concluding on January 1, 2022. The first four years served as a pre-pandemic phase, and the second two years, respectively, served as a pandemic phase.

## RESULTS

In the years leading up to the COVID-19 pandemic, we identified an average of 57 new patients each year; but, after the pandemic began, we were only able to identify 26 new cases annually. However, the baseline characteristics of these people did not change significantly before or during the pandemic. They had a regular distribution of age and BMI. This was the case both before and after the outbreak. This was the situation before to and after the pandemic as well. There were statistically significantly fewer cases of cervical cancer that were found at the period of the pandemic; nevertheless, there was an increase in the number of cases diagnosed at later stages. In all, 21.1 percent of cervical cancers that were identified during the pandemic were at the FIGO stage I, which is a significant decrease from the 39.7 percent of cervical cancers that were detected before the pandemic. FIGO stage III cervical cancers accounted for 34.6 percent of the total population during the first twenty-four months of the pandemic, which is a significant increase from the 22.4 percent that they accounted for before the pandemic (p-value = 0.047). Newly diagnosed patients experienced a significant increase in the number of changes to their treatment plans (12.1 percent pre-pandemic vs. 23.1 percent during the pandemic, p-value = 0.030), postponed surgeries (9.4 percent pre-pandemic vs. 21.2 percent during the pandemic, p-value = 0.011), and radio-chemotherapy treatment changes (12.9 percent pre-pandemic vs. 28.8% during the pandemic, p-value = 0.002).

We identified 160 early-stage malignancies among the 392 patients who presented with cervical cancer throughout the duration of the research. These patients received surgery with the hope of achieving a curative outcome, and they were followed for a period of three years after the operation. During the first two years and four months of the COVID-19 pandemic, a total of 32 patients were infected with the SARS-CoV-2 strain. Table 2 provides a classification of the individuals concerned according to their SARS-CoV-2 status. These patients, like the rest of the cohort as a whole, did not exhibit any significant variations in the features and oncological results they had at the beginning of the study. Twenty-four patients benefitted from hysterectomy performed with robotic assistance, whereas the other patients underwent Wertheim–Meigs hysterectomy performed with the purpose of curing their condition. Even though the Clavien–Dindo score was significantly lower for patients operated on in minimally-invasive techniques (p-value = 0.031), and during the follow-up period, they had significantly more changes in treatment methods or delayed appointments caused by the COVID-19 restrictions, there were no significant differences in the three-year disease-free survival based on surgical treatment method (log-rank p-value = 0.449). This was shown by the fact that there were no significant differences in the In addition, the SARS-CoV-2 status did not have a significant impact on the overall survival rate (the log-rank p-value was 0.608).

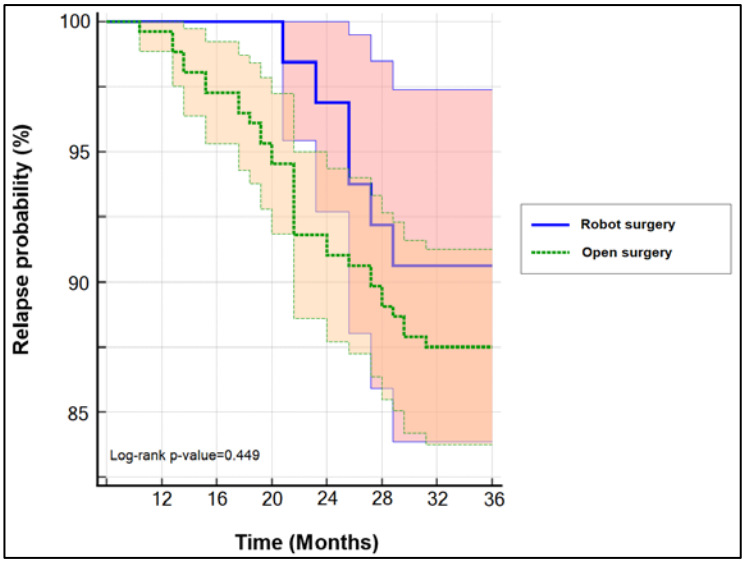


Figure 4. Kaplan-Meyer plot of the three-year disease-free survival in patients with early-stage cervical cancer based on the surgical treatment type.

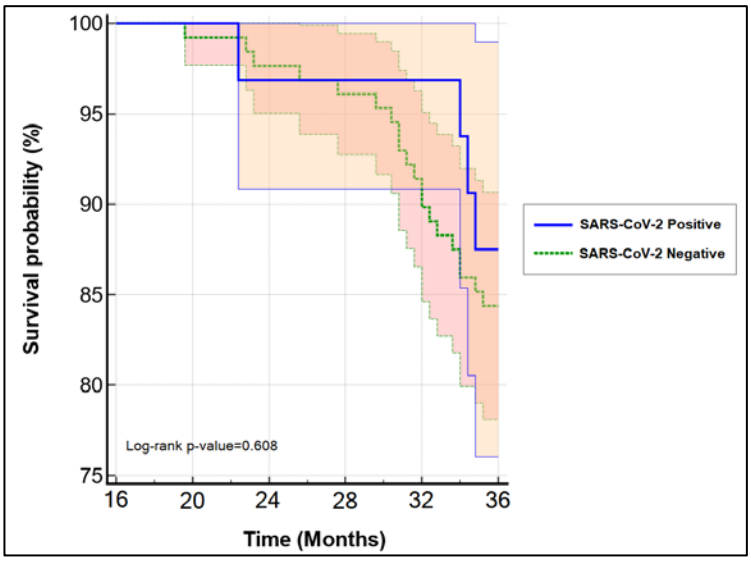


Figure 5. Kaplan-Meyer plot of the three-year survival probability in patients with newly-diagnosed cervical cancer based on SARS-CoV-2 infection status.

During the course of the trial, a risk factor analysis was performed in order to evaluate the independent factors that contributed to death at three years in patients who were newly diagnosed with cervical cancer. This was done in order to evaluate the factors that contributed to death at three years. Significant independent risk factors for death were identified as a big tumor size (two centimeters in diameter or more), cancer recurrence, high-grade histological type, and the number of lymph nodes that were implicated (2). These aspects are important in their own right, despite the fact that they do not interact with one another. On the other hand, infection with SARS-CoV-2 and a Clavien–Dindo score of 3 or higher were not shown to be significant independent risk factors for death at three years (confidence interval [CI] = 0.7–1.9, p-value = 0.246; respectively, CI = 0.9–1.9, p-value = 0.085). These two risk factors were not shown to be significant independent risk factors for death at three years. It does not seem that the changes that were made to medical or surgical plans during the COVID-19 pandemic were independent risk factors that led to undesirable outcomes. This involves delaying treatments such as chemotherapy and radiation as well as surgical procedures.

Table 1. Multivariate regression analysis for the three-years mortality in patients with early-stage cervical cancer.

| Factor | Odds Ratio | Confidence Interval | P-value |
|---|---|---|---|
| Tumor Size (≥2cm) | 1.8 | 1.4–2.5 | 0.022 |
| Relapse | 4.2 | 3.1–5.8 | <0.001 |
| High Grade | 5.1 | 3.3–7.2 | <0.001 |
| SARS-CoV-2 infection | 1.3 | 0.7–1.9 | 0.246 |
| Lymph Nodes (≥2) | 2.9 | 1.6–3.6 | 0.003 |
| Clavien-Dindo (≥3) | 1.5 | 0.9–1.9 | 0.085 |
| Change in treatment plan | 1.3 | 0.9-1.6 | 0.104 |
| Postponed surgery* | 1.1 | 0.8-1.3 | 0.417 |
| Postponed radio-chemotherapy* | 1.3 | 0.8-1.7 | 0.115 |

* Between 1 and 8 weeks

Patients with early-stage cervical cancer were included in the present research, which provides a complete investigation of the impact of the COVID-19 pandemic on medical and surgical therapy, disease-free survival, and overall survival in these patients. The goal of this research is to try to make projections about what the future holds for people who have this particular kind of cancer during the pandemic and to analyze the ramifications of these results for the years to come. Another one of our goals that we were successful in achieving was to determine a number of features within this cohort that enhanced the chance of mortality. One example of this is the existence of the SARS-CoV-2 infection in patients who were diagnosed with cervical cancer. In addition, our study compares the postoperative outcomes of two distinct surgical procedures, namely the conventional open surgery for radical hysterectomy with pelvic lymphadenectomy and the state-of-the-art robotic surgery radical hysterectomy with pelvic lymphadenectomy. Both procedures involve the removal of the uterus and pelvic lymph nodes. Both of these operations are examples of what are known as radical hysterectomies.

## CONCLUSIONS

The COVID-19 pandemic precipitated a healthcare crisis on a scale never before seen on our planet, and it forced the global medical profession to make hasty adjustments. It was essential to provide an immediate reaction in order to facilitate the generation of recommendations that may help doctors. The results of our investigation, on the other hand, suggest that this time period had a substantial influence on the treatment approaches that were used for cervical cancer.

Changes in therapy were documented in 31% of instances, and treatments were halted in 25% of cases, depending on the availability of the healthcare practitioner and the patient's condition regarding SARS-CoV-2. This is despite the fact that the choice of surgical method between traditional hysterectomy and robotic hysterectomy did not affect the disease-free survival of patients with early-stage cervical cancer, nor did the SARS-CoV-2 infection affect the overall survivability of these patients. Rather, the disease-free survival of patients with early-stage cervical cancer was not affected by either of these factors. Therefore, practicing clinicians should absolutely avoid any delays in surgical and medicinal therapy for patients with cervical cancer that are longer than eight weeks, both during and after the COVID-19 pandemic. Delays of this length are considered to be unacceptable. These kinds of delays may constitute a considerable risk to patients' chances of surviving cancer and being disease-free in the long run. It is recommended that this study be reinforced with more research on the impact of the COVID-19 pandemic on the survival rates of patients. This will provide a deeper understanding of the efficiency of the limits imposed during the lockdown as well as the length of time lost due to diagnostic delays as a result of the cancellation of many expert visits.

# CHAPTER 3. THE IMPACT OF SARS-COV-2 PANDEMIC ON PATIENTS UNDERGOING RADIATION THERAPY FOR ADVANCED

# CERVICAL CANCER AT A ROMANIAN ACADEMIC CENTER: A FOUR-YEAR RETROSPECTIVE ANALYSIS

## BACKGROUND

As the COVID-19 outbreak proceeded, hospitals made alterations to their organizational processes in order to better accommodate patients. These adaptations included reducing the number of staff members and repurposing inpatient beds. As a result of this, the staffing levels and bed capacities of all non-COVID departments were lowered, which had an effect on the provision of care for cancer patients who were having treatment with chemotherapy, brachytherapy, or external radiation. During the COVID-19 pandemic, the strategy for the administration of cancer care should be reformed in order to improve patient treatment and follow-up in accordance with the changing recommendations for radiation therapy for gynecological malignancies. This would be done in order to improve patient care. The application of COVID-19 guidelines, on the other hand, presents a number of challenges because to the prolonged constraints imposed by the pandemic conditions, which need direct interaction with humans. This is the case despite the fact that a vaccination campaign against SARS-CoV-2 is now being carried out on a massive scale.

Participants in the study were adult women over the age of 18 who had a confirmed diagnosis of cervical cancer based on cervical screening cytology, colposcopy, and other invasive methods with biopsy, using conventional methods. These women had presented for cancer treatment after having a cancer diagnosis after having presented for cancer treatment. The duration of the research was from January 2018 all the way through January 2022. The study did not adhere to any specific sample procedure, and it included all of the patients in sequential order who were scheduled to get radiation therapy or combination treatment for cervical cancer. In addition, patients who were scheduled for regular follow-up at the gynecologic oncology units of the two hospitals were included in the study provided they satisfied the inclusion criteria. Patients whose test findings and diagnoses could not be independently verified, in addition to those who lacked the needed information, or those who did not volunteer to take part in the present investigation, were not taken into consideration for inclusion in the study.

## RESULTS

Following the matching of inclusion criteria and case-matching by age, a total of 208 patients were selected for the research throughout the period of forty-eight months. This resulted in the formation of two groups: one group consisting of 104 women who were diagnosed with cervical cancer in the 24 months prior to the start of the COVID-19 pandemic, and another group consisting of 104 patients who were diagnosed during the first 24 months of the pandemic. Both groups were given the same treatment for cervical cancer. There was not a statistically significant change in the proportions of body mass index, smoking history, number of parties, place of origin, job, level of income, or civil status during the course of the study. More than thirty percent of the total cohort of patients are smokers. Furthermore, according to the data, the proportion of women who have gone through menopause is approximately fifty percent of those who have gone through post-menopause.

Before the pandemic, there was a total of 31.7 percent of nulliparous women in the cohort. During the pandemic, there was a total of 33.7 percent of nulliparous women (p-value = 0.915). The majority of participants were employed (62.9 percent during COVID-19 compared to 61.5 percent before COVID-19, p-value = 0.564), and the majority of participants were from urban areas, which accounted for 60 percent of all participants. More than eighty percent of the women who took part in the study were married, and the vast majority of them had a salary that fell somewhere in the middle. There were not any statistically significant differences found between the various research groups with regard to the levels of income (p-value = 0.784).

The number of comorbidities that were detected in the groups that were assessed both before and during the pandemic did not significantly change, with hypertension being the ailment that was observed in the majority of persons (80, or 38.4 percent of the total cohort). It was found that squamous cell carcinoma was the histology of cervical cancer in 168 (80.7 percent) of the cases, and there were no significant differences in the groups that were analyzed (p-value = 0.724). In addition, there was a difference in the size of the tumors that were detected before and during the pandemic that was statistically significant. The p-value for this comparison is 0.037, which indicates that sixty-four percent of the tumors that were found in the cohort during the pandemic were larger than three centimeters. Prior to the pandemic, fifty-seven percent of the tumors that were discovered were smaller than three centimeters in size.

Tumorous invasion of the vagina was significantly further advanced in patients who presented for radiation therapy during the COVID-19 pandemic, with 24.0 percent of cases extending to the lower third of the vagina, compared with 12.5 percent of cases before the pandemic (p-value = 0.046). This was a significant increase from the 12.5 percent of cases that occurred before the pandemic. There was no discernible difference in terms of parametrial invasion or tumor grade between the research groups. During the pandemic, patients were found to be presenting with more advanced stages of cancer (14.4 percent vs. 4.8 percent IVA-IVB; p-value = 0.032), as well as more cases of relapse (27.9 percent vs. 16.3 percent; p-value = 0.044). These factors contributed to an increase in the number of patients treated for palliation (63.5 percent vs. 48.1 percent; p-value = 0.034).

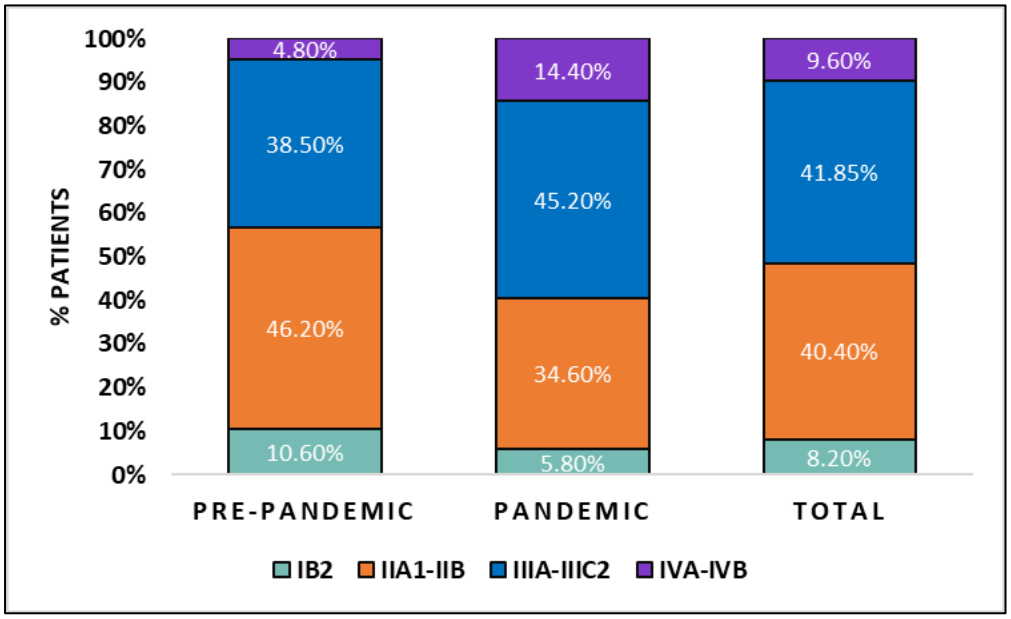


Figure 5. Graphical comparison of patients with radiotherapy-necessitating cervical cancer (IB2-IVB) before and during the COVID-19 pandemic. Cervical cancer staging is reported by the International Federation of Gynecology and Obstetrics (FIGO) staging system.

The number of study participants who had previously been exposed to external beam radiation was 82 (78.8 percent), whereas the number of research subjects who had been exposed to it during the pandemic was 81.7 percent (p-value = 0.601). Patients who were being treated for cervical cancer with radiation therapy experienced anemia in the greatest number (132, or 63.4 percent of the total cohort), followed by leucopenia (127, or 61.0 percent) patients and skin toxicity (107, or 51.4 percent) patients. Anemia was the acute toxicity caused by radiation that was observed in the greatest number of patients. The most common kind of late poisoning, which affected a total of 60 individuals and accounted for 28.8 percent of all cases, had digestive symptoms.

During the COVID-19 pandemic, it was discovered that 22.1 percent of patients had illness progression after finishing the radiation treatment regimen. This number is considerably greater than the 11.5 percent of patients who had disease progression before the pandemic (p-value = 0.045). This was one of the important discoveries that was made. After the pandemic, the majority of referrals came from secondary care (51%; p-value = 0.025), while before the pandemic, the majority of referrals came from primary care (64.4%). There was a 13.5% rise in the number of patients who had been referred to medical experts but did not end up obtaining treatment (p-value = 0.021). This increase occurred throughout the pandemic. There were also substantial shifts in the results of therapy, with 25.0% of patients having adjustments made to their treatment regimens while the pandemic was ongoing, compared to 13.5% of patients before the pandemic (p-value = 0.034). The proportion of patients whose treatment regimens were changed as a result of the pandemic was much higher than it had been before the outbreak. A total of 22 patients, or 21.2 percent, had delayed treatment during the pandemic, and 23.1 percent missed appointments owing to a variety of reasons; this is in comparison to 9.6 percent and 12.5 percent, respectively, before the pandemic (p-values of 0.021 and 0.015, respectively).

After finishing the radiation treatment plan, a Cox regression model was used to investigate the risk factors that might lead to the advancement of the illness. The findings are presented below in descending order of the hazard ratios they indicate. Patients with an advanced FIGO stage of cervical cancer had a 3.39 higher likelihood of disease progression after radiotherapy (CI [2.06–4.21], p-value 0.001), followed by tumor size with an HR of 3.12 (CI [2.24–4.00], p-value 0.001) Patients with an advanced FIGO stage of cervical cancer had a 3.39 higher likelihood of disease progression after radiotherapy (CI [2.06–4.21], p-value 0.001). Patients with advanced FIGO stages of cervical cancer exhibited a 3.39 times greater chance of disease progression after radiation (confidence interval [2.06–4.21], p value = 0.001). Both delaying cancer treatment and failing to keep scheduled appointments, both of which have been linked to the COVID-19 pandemic, have been demonstrated to be substantial risk factors for the disease's progression (hazard ratios of 2.51 and 2.24, respectively). Invasion of the vagina, the patient's age, and the patient's reaction to treatment after three months were among factors that had a significant influence in the development of the disease.

Table 2. Risk factors for disease progression after finishing the radiation therapy regimen.

| Risk Factors | HR | CI | p-value |
|---|---|---|---|
| FIGO stage | 3.39 | 2.06–4.21 | <0.001 |
| Tumor size | 3.12 | 2.24–4.00 | <0.001 |
| Invasion of vagina | 2.58 | 1.82–3.73 | <0.001 |
| Postponed treatment | 2.51 | 1.90–3.46 | 0.001 |
| Missed appointments | 2.24 | 1.18–3.53 | 0.001 |
| Response to treatment at 3 months | 1.66 | 1.09–2.52 | 0.014 |
| Age | 1.35 | 1.01–1.84 | 0.033 |

* FIGO – International Federation of Gynecology and Obstetrics; HR – Hazard Ratio; CI – Confidence Interval.

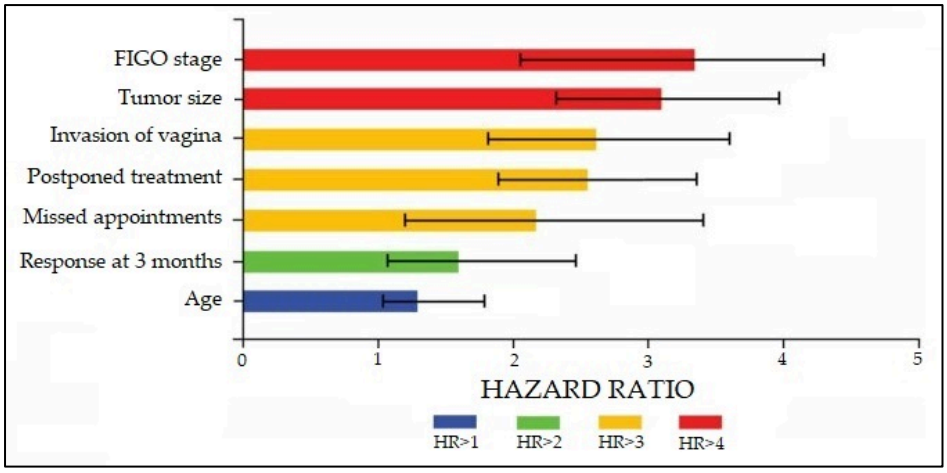

Figure 7. Graphical representation of risk factors for disease progression in patients with cervical cancer undergoing radiation therapy. The likelihood of disease progression is reported as hazard ratio (HR) and confidence interval.

In the current study, it was shown how the COVID-19 pandemic in Romania had an effect on the detection and treatment of cervical cancer in women who were already at an advanced and incurable stage of the disease. This was accomplished by looking backwards at previous events. These findings provide evidence that the majority of hypotheses and predictions suggesting that a significant number of cancer cases were missed throughout the course of the ongoing pandemic are supported by these findings. This was previously observed in the entire population of patients with cervical cancer from Romania during the pandemic. Furthermore, as was previously observed in the entire population of patients with cervical cancer from Romania during the pandemic. A significant number of patients may have missed appointments, intentionally delayed treatment, or intentionally refused treatment after receiving a diagnosis of low-stage cervical cancer. This cancer, despite being curable in the early stages, progressed to an inoperable stage and required treatment with chemotherapy, radiation therapy, or a combination of all three. In addition, we have taken into consideration the possibility that a significant number of patients may have intentionally delayed treatment after receiving a diagnosis of low-stage cervical cancer. We discovered that the chance of cervical cancer patients coming for radiation treatment at a later stage than before the pandemic climbed by about 20 percent as a result of the pandemic. Our investigation brought us to this conclusion.

## CONCLUSIONS

Even though cervical cancer is not one of the most prevalent forms of cancer, it is plausible that a considerable number of cases remained misdiagnosed during the COVID-19 pandemic. This is a possibility despite the fact that cervical cancer is not one of the most common types of cancer. In the event that these people are not identified and treated as soon as humanly feasible, the consequences of missing a diagnosis for them will be far-reaching. After the pandemic restrictions have been eased, it would be appropriate to conduct a thorough screening campaign for cervical cancer, in addition to screening for the other prevalent malignancies that may be detected using screening techniques. This would be appropriate in addition to screening for other cancers that can be detected using screening techniques. In the future, efforts should be aimed toward undertaking a prospective study and following up with current patients who were identified during the COVID-19 pandemic. This is an important step that should be taken. This will contribute to the validation of the predicted outcomes and offer a more precise assessment of the consequences that the pandemic will have on people who have cervical cancer.