

GOPEN ACCESS

Citation: Basta T, Knapp P, Blecharz P, Bodnar L, Gawron I, Babczyk D, et al. (2019) Current management of cervical cancer in Poland— Analysis of the questionnaire trial for the years 2002-2014 in relation to ASCO 2016 recommendations. PLoS ONE 14(1): e0209901. https://doi.org/10.1371/journal.pone.0209901

Editor: Magdalena Grce, Rudjer Boskovic Institute, CROATIA

Received: June 13, 2018

Accepted: December 13, 2018

Published: January 31, 2019

Copyright: © 2019 Basta et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are available in the paper and its Supporting Information files. Additional data may be accessed from the Polish Gynecologic Oncology Society Institutional Data Access (http://ptgo.pl/).

Funding: The study received the funding from Narodowe Centrum Nauki, Poland, N407 152740 https://www.ncn.gov.pl/.

Competing interests: The authors have declared that no competing interests exist.

RESEARCH ARTICLE

Current management of cervical cancer in Poland—Analysis of the questionnaire trial for the years 2002-2014 in relation to ASCO 2016 recommendations

Tomasz Basta¹, Paweł Knapp², Paweł Blecharz³, Lubomir Bodnar⁴, Iwona Gawron¹, Dorota Babczyk¹, Magdalena Piróg¹, Tomasz Kluz⁵, Anna Markowska⁶, Anna Horbaczewska¹, Robert Jach¹*

 Department of Gynecology and Obstetrics, Jagiellonian University Medical College, Krakow, Poland,
 Department of Gynecology and Gynecological Oncology, Faculty of Medicine, Medical University in Bialystok, Bialystok, Poland, 3 Gynecologic Oncology Department, Centre of Oncology, Maria Sklodowska-Curie Memorial Institute, Krakow Branch, Krakow, Poland, 4 Department of Clinical Oncology, Military Institute of Medicine in Warsaw, Warsaw, Poland, 5 Department of Obstetrics and Gynecology, Fryderyk Chopin University Hospital No 1, Faculty of Medicine, Rzeszow University, Rzeszow, Poland, Poland,
 Department of Perinatology and Gynecology, Poznan University of Medical Sciences, Poznan, Poland

* jach@cm-uj.krakow.pl

Abstract

Objectives

To assess the survival of patients with cervical cancer (CC). Since the recommendations concerning cervical cancer management adopted by Polish medical societies do not differ significantly from the ESGO or non-European guidelines, and the fact that evaluation of the system for CC treatment in Poland, as well as the mortality rate of Polish women with CC, which is 70% higher than the average for European Union (EU) countries, justifies the hypothesis that treatment of CC in Poland deviates from the Polish and international recommendations. This article puts forward the current management of cervical cancer in Poland and discusses it in the context of ASCO guidelines.

Material and methods

A survey retrospective multicenter analysis of the medical records of 1247 patients with cervical cancer who underwent treatment for disease and who had completed at least two years of follow-up.

Results

Although concurrent radiotherapy and chemotherapy is a standard treatment of FIGO IB to IVA cervical cancer patients in enhanced- and maximum-resources settings, in our analysis, we found that the percentage of women subjected to chemotherapy was lower than in countries where total survival rates were lower.

Conclusion

Within the IA to II A cervical cancer patients studied group, the methods of treatment remained in line with ASCO guidelines for countries with the highest standard of care.

Although concurrent radiotherapy and chemotherapy is a standard treatment of FIGO IB to IVA cervical cancer patients in enhanced- and maximum-resources settings, in our analysis, we found that the percentage of women subjected to chemotherapy was lower than in countries where total survival rates were lower.

Our findings, together with the inconsistencies within the cervical cancer screening program, may be one of the explanations of poorer survival rate of women with cervical cancer in Poland.

Introduction

Cervical cancer (CC) is the fourth most common cancer type among women. In 2012, the worldwide number of women with CC was around 528 000, of whom 266 000 died. In 85% of cases, CC is diagnosed in developing countries where it is a leading cause of death among women suffering from cancer [1]. A significant difference in incidence and mortality due to CC is observed between low- and middle-income countries and high-income countries [2, 3, 4].

According to World Bank data, Poland is one of the high-income countries [5]. However, results of CC treatment are unsatisfactory. The GLOBOCAN 2012 project places Poland among countries with the highest rate of incidence and mortality due to CC, with the standardized incidence rate (SIR) at 12.2/100 000 and the standardized death rate (SDR) at 5.4/ 100,000 (one of the highest among the surveyed countries). Both SIR and CDR are relatively high compared to other European countries [6]. According to the World Health Organization (WHO), therapeutic options in cervical cancer patients should be selected in line with international, national or institutional guidelines, based on the combination of evidence, availability of trained professionals, equipment facilities and infrastructure [7].

In order to provide evidence-based and resource-stratified global recommendations on the management and palliative care of women with invasive CC, the American Society of Clinical Oncology (ASCO) convened a multidisciplinary multinational panel of experts who produced recommendations reflecting settings diversity. The aim was to develop guidelines that would provide the best medical care to patients with CC and, at the same time, could be adapted to four levels of financial resources [8].

Until the 1990s, the standard treatment of CC at the stage of IIB-IVA according to the International Federation of Gynecology and Obstetrics (FIGO), or in earlier stages with histological factors of unfavorable prognosis, was the use of radiotherapy alone. A rapid increase in the incidence of combination therapy (radio- and chemotherapy) has been since the mid 1990s [9]. Extensive multicenter randomized clinical trials (RCTs) [10,11,12] demonstrated extended survival in patients with advanced CC following radiotherapy with concurrent chemotherapy based on cisplatin compared to radiotherapy alone. On the other hand, recommended management of less advanced stages of CC (FIGO I-IIA), including surgery with or without adjuvant therapy, has not undergone any major changes in the last few decades. The recommendations adopted by Polish medical societies [13, 14] do not differ significantly from the FIGO [15] or non-European guidelines [16,17]. Evaluation of the system for CC treatment

in Poland [18], as well as the mortality rate of Polish women with CC, which is 70% higher than the average for European Union (EU) countries [19], justifies the hypothesis that treatment of CC in Poland deviates from the Polish and international recommendations. This article puts forward the current management of cervical cancer in Poland and discusses it in the context of ASCO guidelines.

Material and methods

The retrospective survey study was conducted in the years 2015–2016. The inclusion criteria were women treated due to CC, who had at least two years of post treatment follow-up data. Eligibility of cases excluded factors such as surgical approach, surgery type or primary treatment. Questionnaires were sent to 24 centers of gynecological oncology providing comprehensive treatment of CC. Completed questionnaires were sent back from 16 centers (Szpital Uniwersytecki w Krakowie, Centrum Onkologii im M. Skłodowskiej-Curie, Świętokrzyskie Centrum Onkologii, Wojewódzki Szpital Zespolony w Kielcach, Szpital Specjalistyczny w Brzozowie, Uniwersytecki Szpital Kliniczny w Białymstoku, Białostocki Ośrodek Onkologiczny, Wielkopolskie Centrum Onkologii, Szpital Kliniczny UM w Poznaniu, Szpital Kliniczny w Lublinie, Gdyńskie Centrum Onkologii, DolnoślAskie Centrum Onkologii, Mazowiecki Szpital Bródnowski, Wojskowy Instytut Medyczny, Szpital Specjalistyczny im. M. Kopernika w Łodzi, Centrum Onkologii w Gliwicach). Of these, 4 centers entered data from 200 patients, 10 centers—25–40 patients, and 2 centers—from 25 patients. The data were collected from 1371 women treated due to CC between 2002 and 2014. The database was designed to capture such data as: clinical staging, primary treatment, complications, imaging, treatment-free survival to the first recurrence, first relapse treatment, complications and imaging associated with this management, treatment-free survival to the second recurrence, second relapse treatment, complications and imaging associated with this management, treatmentfree survival to the third recurrence, third relapse treatment, complications and imaging associated with this management, designed to track the treatment of individuals with CC.All data were reviewed by the main and senior author. Any discrepancies in data were corrected through communication between the study monitor and the individual center. Due to the fact that some essential data were not available, 124 patients were excluded from the database. Finally, data from 1247 patients were analyzed. All authors declare no conflict of interest and no financial support. This work was supported by the National Center of Science (NCN grant no. N407 152740).

Statistical analysis

Data were expressed as a percentage, mean standard deviation or median (interquartile range) unless otherwise stated. The Kolmogorov-Smirnov test was used to assess conformity with a normal distribution. A 2-sided p-value of less than 0.05 was considered statistically significant. Statistical analyses were performed with Statistica 12 (Statsoft, Tulsa, OK, USA).

Results

Patient age ranged from 27–78, with a median age of 54. The median follow-up after diagnosis was 61 (60–67) months. Among 1218 women, squamous cell cancer was diagnosed in 1070 (87.9%), adenocarcinoma in 112 (9.2%), adenosquamosum in 4 (0.3%) and other types in 32 (2.6%) women. Grading of cervical cancer, based on histopathological examination, was as follows: G1–14 (7.8%), G2–115 (64.3%), and G3–50 (27.9%). The distribution of clinical stage was described in Table 1.

FIGO stage	N (1145)	(%)
IA	74	6.5
IB	353	30.8
IIA	123	10.7
IIB	289	25.2
IIIA	19	1.7
IIIB	229	20.0
IVA	20	1.8
IVB	38	3.3

Table 1. Clinical stage of cervical cancer according to the FIGO classification.

https://doi.org/10.1371/journal.pone.0209901.t001

First-line treatment

In the first-line therapy, a surgery was performed in 540 (43%) women (507 cases of radical hysterectomy, (95%); 15 cases of conization, 3% of cases; 11 cases of cervical conization with subsequent radical hysterectomy, 2%. Brachytherapy (BT) was performed in 889 (71%) women and teleradiotherapy (with or without chemotherapy) in 871 (70%) women included in the study (radiotherapy in 194 women, 16%; radiochemotherapy in 677 women, 54%; Detailed analysis of treatment method combinations is presented in Table 2.

Chemotherapy was applied in 727 (58.3%) cases. The most commonly used drug was cisplatin alone (50%), less frequently, cisplatin in combination with 5-fluorouracil (21%) and carboplatin with paclitaxel (16%) (Table 3).

Progression after primary treatment was found in 9.3% of cases. Local recurrence and distal metastases occurred in patients treated with brachytherapy in combination with radiotherapy and brachytherapy in combination with radiochemotherapy, and concerned stages FIGO IB and IIB. The type of cervical cancer recurrence was dependent on the first-line treatment. (Table 4)

Distal metastases were more frequent (67.2%) than local recurrence (31%) (Table 5).

The highest percentage of local recurrences and distant metastases was found in the group treated with brachytherapy (14.7%) in combination with radiochemotherapy (47.4%) (Table 6), as well as FIGO IIB (12.9%) with distant metastases (25.9%) (Table 7).

Second-line treatment

The first recurrence after primary treatment was most often treated with chemotherapy, i.e. in 55 women (47%). The mean time from the end of primary treatment to the start of recurrence

Table 2. Combinations of treatment methods in the first-line therapy of cervical cancer.

First-line treatment	N (%)	Additional brachytherapy N (% after first-line treatment)	Additional radiotherapy N (% after first-line treatment)	Additional chemotherapy N (% after first-line treatment)
Cc	16 (1.2%)	1 (6.3%)	2 (12.5%)	3 (18.8%)
Cc+RH	10 (0.8%)	1 (10%)	-	-
RH	507 (40.7%)	347 (64.3%)	240 (47.3%)	188 (37.1%)
BT	540 (43.3%)	-	518 (95.9%)	463 (85.7%)
RT	111 (8.9%)	-	-	43 (38.7%)
СТ	30 (2.4%)	-	-	-
No treatment	33 (7.7%)	-	-	-

Abbreviations: RH—radical hysterectomy; Cc-cervical conization; BT—brachytherapy; RT—radiotherapy; CT-chemotherapy; RCT-radiochemotherapy;

Chemotherapy	N (191)	%
cisplatin	98	51.3
cisplatin and 5-fluorouracil	42	22.0
paclitaxel and carboplatin	31	16.2
cispltin and topotecan	5	2.6
cisplatin and paclitaxel	2	1.0
cisplatin and carboplatin	2	1.0
cisplatin and gemcitabine	1	0.5
topotecan and indicacine	1	0.5
combinations of schemes	9	4.7

Table 3. Chemotherapy used in first-line treatment of cervical cancer.

https://doi.org/10.1371/journal.pone.0209901.t003

Treatment method	Local recurrence N (42)	Distant metastases N (86)
No treatment	1	2
RH	1	0
RH + BT	3	1
RH + RT	2	0
RH+ RCT	0	2
RH + BT+ RT	2	2
RH + BT+ CT	4	6
RH + BT + RCT	4	6
Cc + BT + RCT	1	0
Cc + RCT	1	0
BT + CT	0	1
BT + RT	1	6
BT	1	0
BT + RCT	17	55
RCT	3	5
RT	1	0

Table 4. Type of cervical cancer recurrence depending on the first-line treatment.

Abbreviations: RH—radical hysterectomy; Cc—cervical conization; BT—brachytherapy; RT—radiotherapy; CT—chemotherapy; RCT—radiochemotherapy;

https://doi.org/10.1371/journal.pone.0209901.t004

FIGO stage	Local recurrence	Distant metastases
IA	2	0
IB	8	11
IIA	4	15
IIB	15	30
IIIA	2	3
IIIB	7	17
IVA	0	1
IVB	0	3

Table 5. Number of cases of cervical cancer recurrence after first-line treatment in relation to the FIGO stage.

Recurrence treatment	N (116)	%
No further treatment	25	21.5
RH	2	1.7
RH + CT	2	1.7
RH + RCT	1	0.9
Cc + CT	1	0.9
Cc + BT + RCT	1	0.9
BT	3	2.6
BT + RCT	1	0.9
RT	15	12.8
СТ	55	47.4
RCT	9	7.8
Cc	1	0.9

Table 6.	Cervical	cancer	recurrence	treatment	(Second-line	therap	y)	۱.
----------	----------	--------	------------	-----------	--------------	--------	----	----

Abbreviations: RH—radical hysterectomy; Cc—cervical conization; BT—brachytherapy; RT—radiotherapy; CT— chemotherapy; RCT—radiochemotherapy;

https://doi.org/10.1371/journal.pone.0209901.t006

treatment in women included in the study was 62 weeks (95% CI: 50–74 weeks; 15.5 months, 95% CI: 12.5–18.5 months). The most common second-line management types were chemo-therapy (47.41%), no treatment (21.6%) and radiotherapy (12.9%) (Table 8).

The most frequent regimen used in the second-line chemotherapy was paclitaxel with carboplatin (27%), followed by cisplatin and 5-fluorouracil (22.1%), and cisplatin and topotecan (13%) (Table 9).

Discussion

In the years 2005–2010, the survival rate in CC patients in Poland, according to the National Health Fund (Narodowy Fundusz Zdrowia, NFZ) was 55%. However, according to the National Cancer Registry (Krajowy Rejestr Nowotworów, KRN), in the years 2003–2005, it was 54%, and according to Eurocare, in the years 1999–2007, it was 53%. The values of comparable indicators in Poland were about 10% lower than average levels in Europe (RSC, according to Eurocare) [20]. According to NFZ data, there were significant differences in survival rates between voivodeships, reaching 20 percentage points (Podlaskie Voivodeship 67%, Lodzkie Voivodeship 45%). There were also discrepancies in these indicators depending on

Treatment	N (76)	(%)
paclitaxel and carboplatin	21	27.6
cisplatin and 5-fluorouracil	17	22.4
cisplatin and topotecan	10	13.2
cisplatin	8	10.5
cisplatin and paclitaxel	6	7.9
paclitaxel	1	1.3
paclitaxel and topotecan	1	1.3
topotecan	1	1.3
ifosfamide	1	1.3
combination of schemes	10	13.2

Second-line treatment	Ν	(%)
No treatment	25	21.5
RH	2	1.7
RH+CT	2	1.7
RH+RCT	1	0.9
Cc+CT	1	0.9
$\overline{Cc + BT + RCT}$	1	0.9
BT	3	2.6
BT + RCT	1	0.9
RT	15	12.9
СТ	55	47.4
RCT	9	7.8
Cc	1	0.9

Table 8. Combinations of second-line treatment.

Abbreviations: RH—radical hysterectomy; Cc—cervical conization; BT—brachytherapy; RT—radiotherapy; CT— chemotherapy; RCT—radiochemotherapy;

https://doi.org/10.1371/journal.pone.0209901.t008

the data source (NFZ data vs. KRN data), which cannot be explained by other data methodology [21]. Treatment of CC at an early stage involves surgery and radiotherapy. Surgical methods are generally reserved for stage IA, IB1, and in some cases, IIA1.

Chemoradiotherapy is a method of choice in the treatment of stages IB2 to IVA. It can also be used in patients who are not eligible for surgery [22, 23]. In guidelines of leading societies (with the exception of the European Society for Medical Oncology- ESMO), radical hysterectomy with pelvic lymphadenectomy, and para-aortic lymph node sampling in selected cases, are recommended in women with an early-stage or locally advanced disease. According to ESMO, radical hysterectomy is not recommended for the early stage of the disease. Microinvasive cervical cancer (stage IA1) without lymphovascular space invasion (LVSI) can be managed with conization or simple trachelectomy in order to preserve fertility, and simple hysterectomy can be offered if the patient does not wish to preserve fertility. In stage IA1 with LVSI, surgical assessment of pelvic lymph nodes should be discussed with the patient, including the sentinel lymph node. This approach provides a much less mutilating procedure for the patient [24, 25, 26].In our study, we found that in the first-line therapy, surgery was performed in 540 (43%) patients (507 cases of radical hysterectomy, 95%; 15 cases of conization, 3% of cases; and 11 cases of cervical conization with subsequent radical hysterectomy, 2%. Taking into account

Table 9.	Type of chemot	herapy in secon	d-line treatment.
----------	----------------	-----------------	-------------------

Type of chemotherapy	N	(%)
cisplatin	8	10.4
cisplatin + 5-fluorouracyl	17	22.0
cisplatin + paclitaxel	6	7.8
cisplatin + topotecan	10	13
paclitaxel	1	1.3
paclitaxel + carboplatin	21	27.2
paclitaxel + topotecan	1	1.3
topotecan	1	1.3
ifosfamid	1	1.3
combination	10	13

that the stage IA to IIA group accounted for 48% of patients, this method of treatment remained in line with ASCO guidelines for countries with the highest standard of care. For women with locally advanced CC, the role of surgery has been debated for many years, and little benefit from such management has been found for most women in stages IB2 to III [27]. Concurrent radiotherapy and chemotherapy is a standard treatment in FIGO IB to IVA in enhanced- and maximum-resources settings [28, 29, 30, 31, 32, 33, 34].

In our analysis, we found that brachytherapy was performed in 71% and teleradiotherapy (with or without chemotherapy) in 70% women included in the study (radiotherapy in 16%; radiochemotherapy in 54%). Chemotherapy was applied in 58% cases. The most commonly used drug was cisplatin (50% of cases), less frequently, cisplatin in combination with 5-fluorouracil (21%) and carboplatin with paclitaxel (16%). In our study population, the percentage of women subjected to chemotherapy was lower than in countries where total survival rates are lower [35]. Perhaps, this observation resulted from the fact that attempts were made not to delay the use of radiotherapy as a result of administrating chemotherapy. In 16% of women, the chemotherapy scheme consisted of carboplatin and paclitaxel, which proves the management of high-income settings, as shown in the ongoing clinical trial [36]. The purpose of this trial is to investigate the influence of the addition of adjuvant carboplatin and paclitaxel after chemoradiotherapy versus concurrent cisplatin and radiotherapy in FIGO IB to IVA patients. An additional phase III trial of concurrent chemotherapy and pelvic irradiation with or without adjuvant carboplatin and paclitaxel is open for high-risk patients with stage IA2, IB, or IIA cervical carcinoma after radical hysterectomy [37].

Strengths of the study

This was the first study investigating CC management in the Polish population. The observation time in this study was longer than that reported in other studies [38], nevertheless, the mean follow- up was 5.5 years.

Limitations of the study

As other population studies based on administrative data [39,40], this study has some limitations related to data availability. Therefore, we were only able to assess tumor-related factors, management and recurrence-free survival. We were not able to consider additional individual factors, in particular, the effects of comorbidities, general health condition and preferences in the treatment. Similarly, we were not able to evaluate other factors related to medical practice, such as local practice of referring patients to an oncology center, potential limitations in healthcare access or patient's adherence to treatment. Therefore, we have no certainty how each of these uncontrolled factors contributed to the observed outcomes. Tracing the extent to which clinical practice coincides with recommendations is a matter to be considered in future research.

Conclusions

Within the studied group of IA to II A cervical cancer patients, the methods of treatment remained in line with ASCO guidelines for countries with the highest standard of care. Although concurrent radiotherapy and chemotherapy is a standard treatment of FIGO IB to IVA cervical cancer patients in enhanced- and maximum-resources settings, in our analysis, we found that the percentage of women subjected to chemotherapy was lower than in countries where total survival rates were lower.

Our findings, together with the inconsistencies within the cervical cancer screening program, may be one of the explanations of poorer survival rate of women with cervical cancer in Poland.

Supporting information

S1 File. English version of the questionnaire conducted in the centres of gynecological oncology.

(DOCX)

S2 File. Polish version of the questionnaire conducted in the centres of gynecological oncology.

(PDF)

S3 File. Manuscript with track changes. (DOCX)

S4 File. Data collected from the centres of gynecological oncology. (DOC)

Author Contributions

Conceptualization: Paweł Knapp, Lubomir Bodnar, Anna Markowska, Robert Jach.

Data curation: Lubomir Bodnar, Magdalena Piróg, Tomasz Kluz, Anna Markowska, Anna Horbaczewska, Robert Jach.

Formal analysis: Paweł Knapp, Lubomir Bodnar, Dorota Babczyk, Anna Horbaczewska.

Funding acquisition: Robert Jach.

Investigation: Anna Markowska, Robert Jach.

Methodology: Paweł Knapp, Dorota Babczyk.

Supervision: Paweł Knapp, Robert Jach.

Writing - original draft: Tomasz Basta, Iwona Gawron.

Writing – review & editing: Paweł Knapp, Paweł Blecharz, Magdalena Piróg, Tomasz Kluz, Anna Horbaczewska, Robert Jach.

References

- International Agency for Research on Cancer: GLOBOCAN 2012 Cervical Cancer: Estimated Incidence, Mortality and Prevalence Worldwide in 2012. http://globocan.iarc.fr/old/FactSheets/cancers/ cervix-new.asp.
- Olson B, Gribble B, Dias J, Curryer C, Vo K, Kowal P, et al. Cervical cancer screening programs and guidelines in low- and middle-income countries. Int J Gynaecol Obstet. 2016; 134: 239–46 https://doi.org/10.1016/j.ijgo.2016.03.011 PMID: 27350227
- Gelband H., Jha P., Sankaranarayanan R., Horton S. Cancer. Disease Control Priorities, third edition, vol. 3, International Bank for Reconstruction and Development / The World Bank, Washington, DC 20433, USA, 2015
- 4. Randall T.C., Ghebre R. Challenges in prevention and care delivery for women with cervical cancer in Sub-Saharan Africa. Front. Oncol. 2016; 28:160
- 5. http://data.worldbank.org/country/poland
- Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015; 136: 359–386

- World Health Organization. Comprehensive Cervical Cancer Control: a guide to essential practice-2nd edition. World Health Organization, Geneva 2014, Switzerland
- Chuang L.T., Temin S., Berek J.S. Management and care of women with invasive cervical cancer: american society of clinical oncology resource-stratified clinical practice guideline summary. J. Oncol. Pract. 2016; 12: 693–696
- Thomas GM. Improved treatment for cervical cancer concurrent chemotherapy and radiotherapy. N Eng J Med. 1999; 340: 1198–1200
- Keys HM, Bundy BN, Stehman FB, Muderspach LI, Chafe WE, Suggs CL 3rd, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. New Engl J Med. 1999; 340: 1154–61 https://doi.org/10.1056/NEJM199904153401503 PMID: 10202166
- Morris M, Eifel PJ, Lu J, Grigsby PW, Levenback C, Stevens RE, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. New Engl J Med. 1999; 340: 1137–43 https://doi.org/10.1056/NEJM199904153401501 PMID: 10202164
- Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. New Engl J Med. 1999; 340: 1144–53 https://doi.org/10.1056/NEJM199904153401502 PMID: 10202165
- Nasierowska-Guttmejer A, Kędzia W, Wojtylak S, Lange D, Rokita W, Jach R, et al. Polish recommendations regarding diagnostics and treatment of cervical squamous intraepithelial lesions according to the CAP/ASCCP guidelines. Ginekol Pol. 2016; 87: 676–682
- Nowak-Markwitz E, Basta A, Kotarski J, Markowska J, Oszukowski P, Sajdak S, et al.; Polish Gynecological Society. Systemic therapy of recurrent or persistent cancer of the cervix. Recommendations of the Polish Gynecological Society. Ginekol Pol. 2015; 86: 712–4
- Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging for carcinoma of the cervix. Int J Gynaecol Obstet 2009; 105: 107–8 https://doi.org/10.1016/j.ijgo.2009.02.009 PMID: 19342051
- Small W Jr, Strauss JB, Jhingran A, Yashar CM, Cardenes HR, Erickson-Wittmann BA, et al. ACR Appropriateness Criteria definitive therapy for early-stage cervical cancer. Am J Clin Oncol. 2012; 35: 399–405 https://doi.org/10.1097/COC.0b013e3182610537
- Siegel CL, Andreotti RF, Cardenes HR, Brown DL, Gaffney DK, Horowitz NS, et al. ACR Appropriateness Criteria pretreatment planning of invasive cancer of the cervix. J Am Coll Radiol. 2012; 9: 395– 402 https://doi.org/10.1016/j.jacr.2012.02.021
- Jach R, Blecharz P, Kozierkiewicz A. Rak szyjki macicy-diagnoza systemu. Polskie Towarzystwo Ginekologii Onkologicznej. Sekcja ds. profilaktyki i leczenia raka szyjki macicy PTGO. Warszawa, 2016
- 19. http://onkologia.org.pl/nowotwory-szyjki-macicy-kobiet/
- De Angelis R, Sant M, Coleman MP, Francisci S, Baili P, Pierannunzio D, et al.; EUROCARE-5 Working Group. Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE–5-a population-based study. Lancet Oncol. 2014; 15: 23–34
- Nowakowski A, Wojciechowska U, Wieszczy P, Cybulski M, Kamiński MF, Didkowska J. Trends in cervical cancer incidence and mortality in Poland: is there an impact of the introduction of the organised screening? Eur J Epidemiol. 2017 Jun; 32(6):529–532 https://doi.org/10.1007/s10654-017-0291-6
 PMID: 28780640
- ACOG practice bulletin. Diagnosis and treatment of cervical carcinomas, number 35, May 2002. Obstet Gynecol. 2002; 99: 855–67 PMID: <u>11978302</u>
- 23. Wiebe E, Denny L, Thomas G. Cancer of the cervix uteri. Int J Gynaecol Obstet. 2012; 119 Suppl 2: S100–9
- Koh WJ, Greer BE, Abu-Rustum NR, Apte SM, Campos SM, Cho KR, et al. Cervical Cancer, Version 2.2015. J Natl Compr Canc Netw. 2015; 13: 395–404 PMID: 25870376
- Marth C, Landoni S, Mahner S, McCormack M, Gonzalez-Martin A, Colombo N Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28:72–83.
- Ebina Y, Yaegashi N, Katabuchi H, Nagase S, Udagawa Y, Hachisuga T, et al. Japan Society of Gynecologic Oncology guidelines 2011 for the treatment of uterine cervical cancer. Int J Clin Oncol. 2015; 20: 240–8 https://doi.org/10.1007/s10147-015-0806-7 PMID: 25800808
- Kokka F, Bryant A, Brockbank E, Powell M, Oram D. Hysterectomy with radiotherapy or chemotherapy or both for women with locally advanced cervical cancer. Cochrane Database Syst Rev. 2015; 7: CD010260
- Morris M, Eifel PJ, Lu J, et al.: Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. N Engl J Med 1999; 340: 1137–43 <u>https://doi.org/10. 1056/NEJM199904153401501 PMID: 10202164</u>

- Keys HM, Bundy BN, Stehman FB, et al.: Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med 1999; 340: 1154–61 https://doi.org/10.1056/NEJM199904153401503 PMID: 10202166
- Peters WA 3rd, Liu PY, Barrett RJ 2nd, et al.: Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk earlystage cancer of the cervix. J Clin Oncol 2000; 18: 1606–13 <u>https://doi.org/10.1200/JCO.2000.18.8</u>. 1606 PMID: 10764420
- Thomas GM: Improved treatment for cervical cancer–concurrent chemotherapy and radiotherapy. N Engl J Med 2000; 340: 1198–200
- 32. Pearcey R, Brundage M, Drouin P, et al.: Phase III trial comparing radical radiotherapy with and without cisplatin chemotherapy in patients with advanced squamous cell cancer of the cervix. J Clin Oncol 2002; 20: 966–7 https://doi.org/10.1200/JCO.2002.20.4.966 PMID: 11844818
- Rose PG, Bundy BN: Chemoradiation for locally advanced cervical cancer: does it help? J Clin Oncol 2002; 20: 891–3, 2002 https://doi.org/10.1200/JCO.2002.20.4.891 PMID: 11844807
- 34. Chemoradiotherapy for Cervical Cancer Meta-Analysis Collaboration: Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: a systematic review and meta-analysis of individual patient data from 18 randomized trials. J Clin Oncol 2008; 26: 5802–12 <u>https://doi.org/10.1200/JCO.</u> 2008.16.4368 PMID: 19001332
- Bodurka-Bevers D, Morris M, Eifel PJ, et al. Posttherapy surveillance of women with cervical cancer: an outcomes analysis. Gynecol Oncol 2000; 78:187–193. https://doi.org/10.1006/gyno.2000.5860 PMID: 10926801
- Zuliani AC, Esteves SC, Teixeira LC, Teixeira JC, de Souza GA, Sarian LO. Concomitant cisplatin plus radiotherapy and high-dose rate brachytherapy versus radiotherapy alone for stage IIIB epidermoid cervical cancer: a randomized controlled trial. J Clin Oncol. 2014; 32: 542–7 <u>https://doi.org/10.1200/JCO.</u> 2013.50.1205
- Srivastava K, Paul S, Chufal KS, Shamsundar SD, Lal P, Pant MC, et al. Concurrent chemoradiation versus radiotherapy alone in cervical carcinoma: A randomized phase III trial. Asia Pac J Clin Oncol. 2013; 9: 349–56 https://doi.org/10.1111/ajco.12078 PMID: 23710586
- Kowalska JD, Wroblewska A, Ząbek P, Firląg-Burkacka E, Kalinowska M, Byczot Z, et al. Barriers to cervical cancer screening exist despite integrating HIV and gynaecological services for HIV-positive women in Poland. Ginekol Pol. 2018; 89(2):68–73 <u>https://doi.org/10.5603/GP.a2018.0012</u> PMID: 29512810
- 39. van der Aa MA, Siesling S, v d Poll-Franse LV, Schutter EM, Lybeert ML, Coebergh JW. Age-specific differences in the treatment of cervical cancer in the east and the south of The Netherlands 1989–2004. Eur J Obstet Gynecol Reprod Biol. 2009; 147: 78–82 https://doi.org/10.1016/j.ejogrb.2009.07.006
- Pearcey R, Miao Q, Kong W, Zhang-Salomons J, Mackillop WJ. Impact of adoption of chemoradiotherapy on the outcome of cervical cancer in Ontario: results of a population-based cohort study.. J Clin Oncol. 2007; 25: 2383–8 https://doi.org/10.1200/JCO.2006.09.1926 PMID: 17557951