Proceedings From the 1st International Conference "Current Concepts and Controversies in Gynecologic and Urologic Oncology"

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Abstract: The N.N. Alexandrov National Cancer Center of Belarus organized a collaborative international conference entitled "Current Concepts and Controversies in Gynecologic and Urologic Oncology" with the International Gynecologic Cancer Society and the United States National Cancer Institute. International, regional, and national experts presented recent developments and local conditions in the treatment of gynecologic cancers. Findings were reviewed with the intent of optimizing the management of women with gynecologic cancers across the Commonwealth of Independent States region. At the end of the conference, a resolution was adopted to identify areas for improvement and future collaborations.

Key Words: Epidemiology, Belarus, Conference

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The 1st International Conference “Current Concepts and Controversies in Gynecologic and Urologic Oncology” was held on April 27 to 29, 2017, in Minsk, Belarus. The Conference was jointly sponsored and organized by the United States National Cancer Institute (NCI), the N.N. Alexandrov National Cancer Centre of Belarus, and the International Gynecologic Oncology Society (IGCS). The goal of this meeting was to create an international educational and scientific platform to accelerate progress in the fields of gynecologic and urologic oncology. There were approximately 220 participants, with representation from 22 countries including the United States, Canada, Israel, Poland, Germany, Bosnia and Herzegovina, Lithuania, Latvia, Turkey, Palestine, Yemen, Russia, Ukraine, Kazakhstan, Uzbekistan, Tajikistan, Azerbaijan, Georgia, Armenia, Turkmenistan, and Belarus. Hereinafter is a brief overview of the gynecologic portion of the conference.

Belarus is a country of 9.5 million people in eastern Europe, on the western border of Russia and the northern border of Ukraine. The Commonwealth of Independent States (CIS) is a regional organization formed by 11 of 15 former republics of the Soviet Union (Fig. 1). The Commonwealth seeks to coordinate efforts in trade, crime prevention, human rights, and other issues. The gross domestic product per capita in Belarus is US $6,710, and it ranges across the CIS from US $14,170 in Russia to US $900 in Tajikistan. Government expenditure on health care is 328 Euro per capita annually, which is significantly lower than the European Union (1905 Euro per capita annually), whereas the number of physicians in Russia, Belarus, and Ukraine (22/100,000) is more than twice the average of the European Union.

Epidemiology of Gynecologic Cancers in Belarus and the CIS

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Cancer Centre presented “Epidemiology of Gynecologic Cancers in Belarus and the CIS Countries.” Cervical cancer is the most common gynecologic cancer in the CIS region representing approximately 7.3% of new cancer cases, and is the fourth common cause of cancer death. Cervical cancer constitutes approximately 5.8% of new cancer cases in Belarus, and approximately 20.5% and 14.0% of the new cancer cases in the Kyrgyzstan and Uzbekistan, respectively (Globocan, 2012). In Belarus, the 1-year mortality is 12.9%, compared with 31% in Armenia and 24.5% in Kyrgyzstan. Patients often present with advanced stage (III–IV) disease: 29.2% in Belarus, 67.1% in Armenia, and 40.5% in Kyrgyzstan.

Endometrial Cancer comprises 8.5% of new cancer cases in the CIS countries. Approximately 6.0% to 12.0% of the new cases occur in Kyrgyzstan, Moldova, Russia, Belarus, Ukraine, Armenia, and Tajikistan. Approximately 2.3% of the estimated new cases and 1.0% of the cancer deaths occurred in Azerbaijan. One-year mortality rates vary widely across the region from 40.2% in Armenia to 6.4% in Belarus. Similarly, presentation with stages III to IV disease varies from 49.0% in Azerbaijan to 11.9% in Kazakhstan and 12.7% in Belarus.

In 2012, ovarian cancers comprised 5.2% of new cancer cases and 5.6% of cancer deaths among women in CIS countries. Incidence rates are highest in Russia, Belarus, and Ukraine, whereas mortality rates are highest in Kazakhstan, Russia, and Ukraine. Armenia sees the highest 1-year mortality rates (47.5%), whereas the lowest are in Uzbekistan (13.8%).

**IGCS Future Perspectives**

Mary Eiken, RN, MS, CEO of the IGCS, presented an overview of the society and current opportunities for collaboration with the CIS region. The IGCS is seeking to develop alliances with regional societies. These partnerships will bring together the leaders and members of various organizations, allowing for closer dialogue and idea sharing in a forum for information and collaboration. The IGCS offers to share its resources to help the Strategic Alliance Membership improve the outcomes for women with gynecologic cancers internationally.

Dr Thomas Randall from the US NCI Center for Global Health presented the IGCS Global Educational Initiative. Details of this initiative can be found on the IGCS website, [https://igcs.org/education-resources/global-curriculum/](https://igcs.org/education-resources/global-curriculum/). Gynecologic oncologists and other specialists from CIS countries were encouraged to become involved this initiative.

Dr Edward Trimble, Director of the US NCI Center for Global Health, provided an overview of the Gynecologic Cancer InterGroup (GCIG), including priorities and perspectives for the future. The aim of the Gynecologic Cancer InterGroup is to enhance the global impact of clinical trials in gynecologic cancer by promoting international cooperation, promoting clinical research, performing studies in rare...
tumors, stimulating evidence-based medicine, and supporting educational activities.

**Cervical Cancer**

Dr Thomas Randall reviewed the use of human papillomavirus (HPV) testing for cervical cancer screening, including the natural history of HPV infection in women, test characteristics, testing in a vaccinated population, strategies with comparable risk, cost-effectiveness, self-sampling, and management of women with a positive HPV test. The evidence supports HPV DNA testing for both new and established cervical cancer screening programs.

Dr Edward Trimble reviewed the biology of HPV infection, the history of the HPV vaccine, and the current recommendations for HPV vaccination.

Dr Kathleen Schmeler from the Department of Gynecologic Oncology and Reproductive Medicine at The University of Texas MD Anderson Cancer Center presented several cervical cancer quality improvement and research initiatives, including (1) Project ECHO (Extension for Community Healthcare Outcomes), which uses videoconferencing to link academic faculty with clinicians in low resource areas; (2) Ongoing research and the current evidence for less radical and fertility sparing surgeries were reviewed, including the preliminary results of the ConCerv trial and the design of the SHAPE and GOG278 trials; and (3) a video course entitled in the management of high-grade cervical dysplasia and early cervical cancer.

Dr Olga Matylevich, Leading Research Scientist of the Gynecologic Oncology Department at N.N. Alexandrov National Cancer Centre, presented the “Impact of the Treatment Standardization on Survival of Cervical Cancer Patients in Belarus.” She reported on 14,220 patients from the Belarusian Cancer Registry diagnosed with cervical cancer between 2000 and 2015. Overall 5-year survival was compared between patients diagnosed in 2001 to 2007 and 2008 to 2015, to evaluate the effect of the implementation of NCI guidelines in 2007 mandating the concurrent use of chemotherapy with radiotherapy in cervical cancer treatment. The overall 5-year survival rate (2000–2015) was 0.583 (95% confidence interval [CI], 0.575–0.592), with a statistically significant difference in urban and rural patients (0.614 [95% CI, 0.603–0.624] vs 0.511 [95% CI, 0.504–0.535]; P < 0.0001). Survival rates before and after implementation of guidelines did not prove to be significantly different (0.577 [95% CI, 0.565–0.589] vs 0.595 [95% CI, 0.582–0.608]; P = 0.194). When analyzed by cancer stage, the survival rate following the guideline implementation did not change for stage I, was 5% lower for stage II, and was 10% higher for stage III disease. The reason for these surprising results is unclear and will be reevaluated in 2020 when all patients included in this study can be assessed for 5-year survival. Further studies into the disparate survival rates between urban and rural patients are needed.

Dr Aleksey Shevchuk, Leading Research Scientist of the Gynecologic Oncology Department at the P.A. Herzen Moscow Oncology Research Institute, performed a live laparoscopically assisted vaginal radical trachelectomy, which was broadcast into the auditorium for viewing and a question and answer session. He then reviewed the experience of radical trachelectomy at his institution. From 2005 to 2017, 173 patients with stage IA1 (lymph-vascular space invasion+) to IIA cervical cancer underwent radical abdominal trachelectomy (n = 119, 68.8%), radical vaginal trachelectomy (n = 25, 14.4%), or radical laparoscopic trachelectomy (n = 29, 16.7%). Radical abdominal trachelectomy was done in 89 (76.7%) patients with uterine artery preservation and in 30 (25.3%) without uterine artery preservation. A total 9 recurrences were documented with 7 (8.9%) after radical abdominal trachelectomy, 1 (4%) after radical vaginal trachelectomy, and 1 (3.3%) after radical laparoscopic trachelectomy. It was emphasized that for those women attempting pregnancy, collaboration is needed between oncologists and obstetricians. Future studies should explore the role of simple trachelectomy with pelvic lymphadenectomy for tumors less than or equal to 2 cm, sentinel node detection, and neoadjuvant chemotherapy with radical trachelectomy for young patients with tumors greater than or equal to 2 cm.

Professor Albert Singer, PhD, FRCOG, University of London, presented a new mobile colposcope (MobileODT) that includes a cloud-connected system for ongoing quality assurance, supportive supervision, referral tracking, patient engagement, and real time data analytics for administrators and policymakers.

**Endometrial Cancer**

Dr Wendel Nauman, Professor of Gynecologic Oncology at the Levine Cancer Institute in Charlotte, North Carolina, presented “Minimally Invasive Surgery for Endometrial Cancer,” covering the technical aspects and complications of laparoscopic surgery, as well as the clinical trial data informing the role of lymphadenectomy in endometrial cancer was reviewed.

Dr Sergey Taranenko from the Gynecologic Oncology Department at N.N. Alexandrov National Cancer Centre presented “Advantages of Laparoscopic Surgery in Endometrial Cancer Patients” including an experience of the Gynecologic Oncology Department of the National Cancer Center of Belarus. Over 3 years, 746 patients underwent hysterectomy, including 36 operations with pelvic lymphadenectomy. The average operative time was 73 (range, 40–130) minutes, and the average blood loss was 52 (range, 15–330) mL. Complications included conversion to open surgery in 4 cases, bladder injury in 2, large bowel injury in 1, and postoperative bleeding in 1. Clinical examples of operations in patients with a body mass index of greater than 38 were shown as well as a video demonstrating the surgical technique.

Dr Sergey Mavrichev, head of the Gynecologic Oncology Department at N.N. Alexandrov National Cancer Centre, reviewed “Management of Endometrial Cancer Stage I Patients According to the Risk Factors: Optimal Approach.” The literature regarding the role of a regional lymphadenectomy and the role of adjuvant radiation therapy in the management of endometrial cancer was reviewed. A retrospective analysis of 5055 patients in Belarus with stage I endometrial cancer diagnosed between 2006 and 2010 was presented. Of these patients, 3767 had low-risk disease, 920 had intermediate-risk disease, whereas 224 had high-risk disease, and 144 had metastatic disease at presentation. The frequency of a local recurrence for patients with low-risk disease after simple hysterectomy with BSO was 1.4%, whereas after simple hysterectomy with BSO.
hysterectomy with BSO followed by radiation therapy was 2.9%. Based on these findings, regional lymphadenectomy in patients with low-risk endometrial cancer is not recommended, whereas patients with intermediate- and high-risk disease are recommended to undergo pelvic and para-aortic lymphadenectomy. Furthermore, they found that among women with low-risk disease, radiation therapy improved survival for women with stage I, grade 2 disease with myometrial invasion ($P = 0.0005$), but not for women with stage I, grades 1 to 2 disease without myometrial invasion ($P = 0.559$). For stage I, grade 1 patients with myometrial invasion, adjuvant radiotherapy improved overall survival but not progression-free survival ($P = 0.0005$ and $P = 0.541$, respectively). The second prospective randomized trial from Belarus confirmed that for patients with stage I, grades 1 to 2 disease without myometrial invasion, external beam radiotherapy did not improve survival, whereas in similar patients with myometrial invasion, there was a trend toward improved survival with external beam radiotherapy. In our study, lymph-vascular space invasion was an important prognosticator for patients with stage I, grade 1 disease; these women had improved survival when treated with brachytherapy ($P = 0.0004$). Further trials are ongoing to better define optimal treatment recommendations for patients with endometrial cancer in Belarus.

Dr Valentina Suslova from the Radiology Oncology Department at N.N. Alexandrov National Cancer Centre presented “The Role of Adjuvant Brachytherapy in the Management of Endometrial Cancer in Stage I Patients.” Two techniques of brachytherapy were presented: (1) high dose rate brachytherapy, delivered as 2 weekly 8.5 Gy fractions for a total dose of 17 Gy; and (2) pulsed dose rate brachytherapy, 1 pulse per hour, a daily dose 10Gy delivered in 3 weekly fractions for a total dose of 30 Gy. Areas identified for further study include whether it is necessary to irradiate the entire vagina or just the upper one third of the vagina, what mode of fractionation is optimal, and the optimal single and total local doses. The implications of the findings from PORTEC2 were reviewed, again demonstrating that important questions remain in the use of adjuvant brachytherapy for women with endometrial cancer.

Dr Jubilee Brown, Professor of Gynecologic Oncology at the Levine Cancer Institute in Charlotte, North Carolina, presented “Sentinel Lymph Node (SLN) Sampling in Gynecologic Cancers,” including video demonstrations of SLN mapping. The data are compelling for adoption of sentinel lymph node biopsy in the surgical management of early-stage cervical cancer, whereas the role in endometrial cancer surgery is still being defined. Recommendations for learning and adoption of this novel technique were reviewed. Important research questions include how should patients with micrometastasis be managed, how can one best reduce false-negative results, and what combination of dyes are optimal?

Dr Jubilee Brown also reviewed the diagnosis and treatment of Gestational Trophoblastic Neoplasia (GTN). Diagnosis, staging, identification of a false positive hCG test, the cellular biology of GTN, and risk stratification were reviewed. A case was made for a greater awareness of the role of surgery in the management of GTN.

**Ovarian Cancer**

Dr Wendel Naumann reviewed chemotherapy options for ovarian cancer based on a systematic review of the literature. Recent clinical trial results and the role of bevacizumab in the treatment of ovarian cancer were highlighted.

Dr Jubilee Brown addressed the role of targeted therapy in ovarian cancer treatment, including a review of checkpoint inhibitors and other mediators of chemotherapy resistance. The functions of these inhibitors as well as the results of recent targeted therapy trials in gynecologic cancers were reviewed.

Dr Edward Trimble provided an overview of hyperthermic intraperitoneal chemotherapy including the clinical
trial data supporting its use in ovarian cancer. Dr Jubilee Brown presented contemporary data regarding neoadjuvant chemotherapy (NACT) in ovarian cancer treatment from several international clinical trials. A review of these data show that the primary goal of initial management of epithelial ovarian cancer should be to perform a complete resection with no residual disease at the end of surgery; this seems to be more important than the timing of surgery. Postoperative complications and mortality rates were significantly lower and rates of complete macroscopic resection were higher with NACT while progression-free survival and overall survival were equivalent whether the patient underwent primary surgery followed by chemotherapy or NACT followed by surgery.

Dr Elena Dolomanova, Chief of Gynecologic Oncology Department at N.N. Alexandrov National Cancer Centre, presented retrospective single center data regarding tumor reductive surgery for ovarian cancer from the N.N. Alexandrov National Cancer Center. Most patients with advanced ovarian cancer in Belarus are referred to this center. Over the past 10 years, overall survival in patients with advanced ovarian cancer increased by 15%, from 38.5% in 2006 to 54.9% in 2016. In 2016, 215 cytoreductive surgeries were performed; 82% of the patients underwent primary debulking surgery, and 18% underwent NACT with interval debulking surgery. Complete tumor resection was achieved in 114 patients (53%), optimal debulking in 49 patients (22.8%), suboptimal debulking in 10 patients (4.6%), nonoptimal debulking in 38 patients (17.7%), and exploratory laparotomy only in 4 patients (1.5%). Five-year survival for these women was as follows: complete cytoreductions, 71.1%; optimal cytoreductions, 32.3%; and nonoptimal cytoreductions, 30.6% (Fig. 2). Treatment at a high-volume specialty center seems to optimize outcomes for women with advanced ovarian cancer in Belarus.

Dr Anna Plotkin, a pathologist with Trillium Health Partners affiliated with the University of Toronto, presented challenges with the current approach to classification of endometrial cancer. Reproducible diagnosis is the key to standardization of treatment options. Molecular classification of the endometrial cancer and the use of new classifiers to improve reproducibility of the diagnosis of endometrial cancer were discussed. The role of the pathologist has evolved far beyond just providing histological diagnosis. Moreover, the role of pathologists in the early diagnosis of hereditary endometrial cancer was discussed, specifically Lynch syndrome emphasizing immunohistochemical and molecular studies.

Vulva Cancer

Dr Dmitry Rovsky from the Gynecologic Oncology Department at N.N. Alexandrov National Cancer Centre presented the results of surgical treatment for vulvar and vaginal cancer including reconstructive surgery. In Belarus, there are 140 to 170 cases of vulvar cancer annually. In 2016, the total number of cases was 163, representing 2.8 per 100,000 female population. The stage distribution was stage I (n = 90, 55.2%), stage II (n = 33, 20.2%), stage III (n = 28, 17.2%), and stage IV (n = 10, 6.1%). The 5-year survival was 75.7% for stage I, 55.3% for stage II, 27.5% for stage III, and 14.2% for stage IV disease. Several types of reconstructive surgery were reviewed, and 3 cases of primary vaginoplasty with transverse rectus abdominis musculocutaneous flap were presented.

Dr Kathleen Schmeler presented “Ensuring Surgical Safety and Quality.” She highlighted the importance of creating a culture of safety and quality versus blaming individual physicians for medical errors. She described the process of reviewing all quality metrics monthly with all physicians with full transparency, creating leadership positions related to safety/quality, and the importance of collaboration and working as a team.

Tumor Board

A tumor board with audience participation was moderated by Dr Wendel Naumann. The cases reviewed generated discussion regarding the optimal treatment of locally advanced cervical cancer as well as stage IB grade 2 endometrial carcinoma. This forum allowed for interactive
discussions regarding different treatment patterns between the different regions.

**Pathology Workshop**

A workshop was held reviewing the approach to diagnosis of common neoplasms in gynecological pathology. Participants included Drs Anna Plotkin and Anna Portyanko, Head of the Republican Molecular Genetic Laboratory of Carcinogenesis at N.N. Alexandrov National Cancer Centre; Alexander Dubrovsky, Head of the Department of Pathology at N.N. Alexandrov National Cancer Centre; and Juriy Rogov, Head of the Department of Pathology Belarusian Medical Academy of Postgraduate Education. The synoptic reporting of all malignant cases was reviewed including the key elements to be included in the gross and microscopic descriptions. Challenging cases were presented with the latest updates in immunohistochemical and molecular profiling. The workshop concluded with a discussion highlighting the importance of team work between clinicians and pathologists to ensure correct diagnosis and quality reporting for each patient. Strategies to optimize gynecologic cancer pathology in Belarus were discussed.

**Resolution**

At the close of the conference, a resolution presenting opportunities for quality improvement in the region based on evidence reviewed was presented and unanimously adopted (Fig. 3).

**Summary**

Many challenges remain in the management of gynecologic malignancies across the CIS region. The 1st International Conference “Current Concepts and Controversies in Gynecologic and Urologic Oncology” provided a platform to generate ideas and opportunities to work collaboratively to improve the prevention, early detection and treatment of gynecologic malignancies.