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Meeting Report

Report from the 36th Annual Meeting of the Korean Society of Gynecologic Oncology (KSGO)

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INTRODUCTION AND OVERVIEW

On April 17, 2021, the 36th Spring Conference of the Korean Society of Gynecologic Oncology (KSGO) was held. Owing to the coronavirus disease 2019 (COVID-19) pandemic, the conference was held in a virtual format. With its informative and interesting composition, it was a meaningful opportunity for a large number of 372 delegates. A total of 31 speakers addressed 13 scientific sessions, and 70 E-poster abstracts were presented. The conference was chaired by Dr. Young Tae Kim, the president of KSGO, and was moderated by Dr. Dae Woo Kim, the secretary general of KSGO (**Fig. 1**). The immediate past-president, Dr. Seung Cheol Kim and the immediate past-secretary general, Dong Hoon Suh, were awarded appreciation plaques (**Fig. 2**).

Fig. 1. (A) Opening remark by Dr. Young Tae Kim, President of KSGO. (B) The main venue of the 36th Annual Meeting of KSGO.
KSGO, Korean Society of Gynecologic Oncology.

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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Conceptualization: K.Y.T.; Data curation: K.J.H., N.J.J., E.K.J.; Project administration: K.Y.T.; Writing - original draft: K.J.H., N.J.J., E.K.J.; Writing - review & editing: K.J.H., N.J.J., E.K.J., K.Y.T.

Fig. 2. (A) Appreciation ceremony for the immediate past-president, Seung Cheol Kim and the (B) immediate past-secretary general, Dong Hoon Suh.

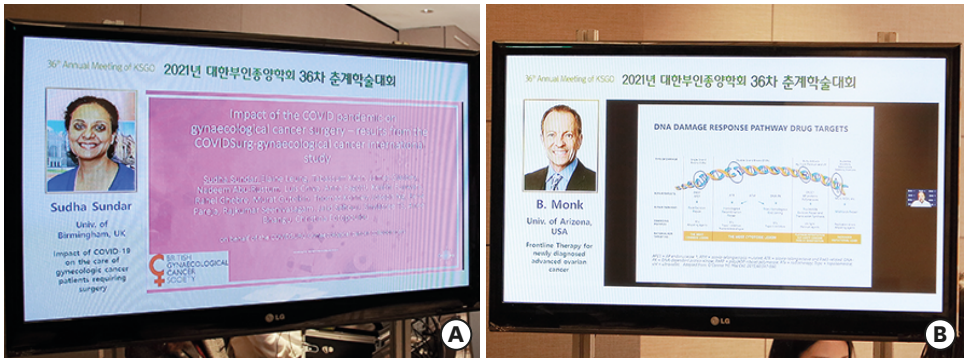

Fig. 3. (A) Virtual lectures of Invited international speakers, Dr. Sudha Sundar from University of Birmingham, UK and (B) Dr. Bradly Monk from university of Arizona, USA.

In Special Lecture session, Dr. Sudha Sundar from University of Birmingham presented how COVID-19 affects the treatment of gynecological cancer patients who require surgery (**Fig. 3A**). At Policy Forum, the topic of evaluating and improving the surgical excellence of ovarian cancer was presented and actively discussed by panelists. Three international speakers were invited to the plenary session and shared their work and updates in gynecologic oncology. In Luncheon symposium session, Dr. Bradly Monk from university of Arizona talked about frontline therapy for newly diagnosed advanced ovarian cancer (**Fig. 3B**).

In the afternoon, there were 2 online channels. In Channel 1, Focused Plenary sessions were dedicated to 10 topics which were selected through strict academic review among the previously submitted abstracts. In Channel 2, a collaborative presentation by academic organizations closely related to the KSGO was made on topics which are updated recently, with masters in the field of pathology, radiation oncology, and chemotherapy (**Fig. 4**). The last, but not the least session of the meeting consisted of three cases of interactive tumor board review in which three expert panels discussed updated treatment options with the audience who were able to show their opinions by simultaneous electronic votes.

This report summarizes the main topics and highlights of each session.

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Fig. 4. Scenes from the Meeting of Korean Society of Gynecologic Oncology.

SPECIAL LECTURE

1. Impact of COVID-19 on the care of gynecologic cancer patients requiring surgery

Dr. Sudha Sundar from Univ. of Birmingham gave a brief overview of the results of COVID Surg-gynacecological cancer international study, a multicenter, international, observational cohort study, to assess the 30-day COVID-19 infection rate in patients with gynecological cancer following elective cancer surgery [1]. From 4,472 patients who underwent gynecological cancer surgery, 2.27% were diagnosed with COVID-19 infection and a 1.18% mortality rate was observed, which was not significantly higher than the previous database before the pandemic. This study provided evidence for performing elective surgery for gynecologic cancer in the era of the COVID-19 pandemic.

2. COVID-19 pandemic and cancer management, clinical trial, and vaccination

Dr. Soo Jin Park from Seoul National University Hospital presented on cancer patient treatment, clinical trials, and vaccination during the COVID-19 era. In the case of cancer patients with confirmed COVID-19, one to four weeks of postponement may be considered for gynecological cancer surgery, and in the case of radiation therapy, a treatment pause should be considered. Physicians should consider holding chemotherapy for at least 10 days, and it is recommended to use granulocyte colony-stimulating factor after fever disappears. It is recommended that clinical trials continue in most situations when it is judged that benefits outweigh the risks according to the sponsor's guidelines.

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POLICY FORUM: SURGICAL QUALITY OF OVARIAN CANCER

1. Surgical quality of ovarian cancer: how to evaluate and improve?

Dr. Suk-Joon Chang from Ajou University gave an important lecture on the quality evaluation and improvement of ovarian cancer surgery. Although the role of surgery is important in ovarian cancer treatment, it is difficult to evaluate the quality of surgery objectively in the real clinical settings. Recently, the European Society of Gynaecological Oncology (ESGO) has created a program to certify institutions with high quality of surgery for advanced ovarian cancer and is attempting to establish objective authentication using 10 quality indicators [2]. The 10 certification indicators include QI 1: Rate of Complete Surgical Resection; QI 2: Number of Cytoreductive Surgeries Per Center and Per Surgeon Per Year; QI 3: Surgery Performed by a Gynecologic Oncologist or a Trained Surgeon Specifically Dedicated to Gynecological Cancer Management; QI 4: Center Participating in Clinical Trials in Gynecologic Oncology; QI 5: Treatment Planned and Reviewed at a Multidisciplinary Team Meeting; QI 6: Required Pre-operative Workup; QI 7: Pre-operative, Intra-operative, and Post-operative Management; QI 8: Minimum Required Elements in Operative Reports; QI 9: Minimum Required Elements in Pathology Reports; and QI 10: Structured Prospective Reporting of Post-operative Complications.

PLENARY SESSION I

1. Drug repositioning for ovarian cancer targeting mevalonate pathway

The first plenary session was opened by Dr. Yusuke Kobayashi from Keio University. Dr. Kobayashi presented how statins, one of the most frequently prescribed medications for dyslipidemia, may help treat ovarian cancer by targeting the mevalonate pathway. This was introduced in the concept of drug repositioning, which is increasingly becoming an attractive proposition because it involves the use of compounds that have already been completed the evaluation of toxicity profiles [3]. Data from The Cancer Genome Atlas (TCGA) showed increased activity of the mevalonate pathway in ovarian cancer patients whereas the pathway was consistently down-regulated in normal samples [4]. In in vivo experiments with ovarian cancer cell lines, a number of mevalonate pathway inhibitors demonstrated concentration-dependent inhibitory effects on cell proliferation [5]. This inhibitory effect was also shown by statin, HMG-CoA reductase inhibitor, and was augmented when given with paclitaxel or carboplatin together, showing synergistic inhibitory effects. Not only in in vivo studies, but also in animal models, mogp-TAg transgenic mouse models, which mimic serous tubal intraepithelial carcinoma (STIC), demonstrated decreased tumor weights after they were given statins. These inhibitory effects of statins were most significantly demonstrated in serous and clear cell ovarian carcinomas among others. The study concluded that statins may have anti-tumor activity against epithelial ovarian cancer, especially serous and clear cell carcinomas, and showed potential benefits that may be derived from its drug repositioning.

2. Novel nanomedicine for epithelial ovarian cancer: cathepsin B-cleavable peptide-conjugated doxorubicin prodrug

The second plenary session was carried out by Dr. Soo-Young Jeong from Hallym University. Dr. Jeong presented how nanoparticles may help deliver anti-cancer drugs in a more efficient way and thereby improve its therapeutic efficacy. Cathepsin B is a member of lysosomal cysteine proteases and involves in intracellular proteolysis. It is known to be overexpressed in various types of cancer and is recently utilized as a selective diagnostic marker [6]. Her

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research team developed carrier-free nanoparticles of cathepsin B-cleavable peptide that conjugates with doxorubicin prodrug. When administered to HeyA8 and HeyA8-MDR cell lines, doxorubicin that is conjugated with cathepsin B-cleavable peptide was shown at a high concentration in intracellular nucleus in HeyA8 cell lines but was distributed in cytoplasm in normal cell lines on confocal microscopy. On the other hand, unconjugated doxorubicin was concentrated in the nucleus both in cancer cell lines and normal cell lines. This suggests the selective distribution of nanoparticle-conjugated anti-cancer drugs in different cell lines, which may provide means to reduce unwanted cellular toxicity in normal cells. This was also demonstrated by decreased cell viability in both cancer cells and normal cells when they were treated with unconjugated doxorubicin, whereas only cancer cells illustrated decreased viability when treated with doxorubicin conjugated with cathepsin B-cleavable peptide. The cell viability of normal cells remained steady. This desired accumulation of nanoparticle-conjugated doxorubicin was also demonstrated in animal model studies. When evaluated with fluorescent microscope on orthotopic ovarian cancer mouse models with HeyA8 cell lines, doxorubicin conjugated with cathepsin B-cleavable peptide was concentrated in tumor tissues at almost 3 to 4 times higher concentrations than unconjugated doxorubicin. The therapeutic efficacy of conjugated doxorubicin remained similar in comparison to unconjugated doxorubicin. In summary, the study demonstrated how novel nanoparticles may allow precise targeting of tumor cells, which consequently achieves enhanced drug delivery and also reduces side effects and drug resistance.

3. Multi-Omics and therapeutically applicable research of ovarian cancer (MOTAROC)

The next session was presented by Dr. Gang Chen from Tongji Medical College in China. He introduced various laboratory techniques from a number of landmark multi-omics studies. He termed the concept of applying these techniques as MOTAROC. Moving from the traditional treatment paradigm of using non-selective cytotoxic agents to selective, genomic and targeted agents for the treatment of ovarian cancer patients, scientists have been able to achieve not only the enhancement of therapeutic effects but also the prolongation of patient survival. Studies utilizing organoids platform, 3-dimentional microfluidic culture, patient-derived xenograft, reverse phase protein microarray (RPPA) are among the examples of such endeavors. In order to benefit from such techniques, precise molecular characterization of patient tumor such as histopathologic, genomic, transcriptomic, proteomic, immunologic and metabolomics analysis should be preceded. By accomplishing such characterization, scientists were able to identify one of the mechanisms by which resistance to poly-ADP ribose polymerase (PARP) inhibitors develop. Studies published in *Science Translational Medicine* in 2017 and in *Cancer Cell* in 2018 showed that specific molecular signaling pathway mediates the development of resistance to PARP inhibitors [7,8]. They found that PARP inhibitors and RAS/mitogen-activated protein kinase (MAPK) kinase (MEK) inhibitor synergistically suppress the growth of tumor cells in epithelial ovarian cancer. Furthermore, researchers have been able to achieve the identification of the relationship between homologous recombination deficiency (HRD) and bromodomain containing 4 (BRD4) proteins and found the inhibition of BRD4 induces HRD regardless of the mutational status in BRCA 1/2, TP53, RAS, or BRAF. This warrants further investigation on the potential usage of BRD4 for ovarian cancer patients with homologous recombination proficiency. As PARP inhibitors are now becoming an important axis in the treatment of ovarian cancer, such studies provide important clues to understand the relationship between PARP inhibitors and HRD status, which is invaluable in the current time.

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PLENARY SESSION II

1. Risk of adverse obstetric outcomes in patients with a history of endometrial cancer: a population-based cohort study

Dr. Seung-Hyuk Shim from Konkuk University presented the results of his nation-wide cohort study on the relationship between fertility-sparing treatment for early endometrial cancer and obstetric outcomes. In order to perform his analysis, he used the data from the Korean National Health Insurance Service. A total of 246 women who had been treated in any form of progestin therapy for early endometrial cancer between 2009 and 2016 prior to delivery were identified. These women were compared to 3.2 million women who delivered without any history of endometrial cancer during the same period of time. He identified that those with the history of progestin therapy for endometrial cancer had higher relative risk ratios for multifetal gestation, delivery by cesarean section, and preterm delivery compared to those women without endometrial cancer. However, the history of endometrial cancer treatment did not increase the risk of preeclampsia, gestational diabetes or any other adverse obstetric outcomes. When sensitivity analysis excluding multifetal gestation was performed, the authors found that the risk of preterm birth was not increased. It also revealed similar rates of preeclampsia, gestational diabetes, placenta previa, placenta accrete and the incidence of vacuum delivery. In conclusion, the study showed the increasing trend of childbirth in endometrial cancer patients after fertility-sparing treatment and comparable obstetric outcomes between those who had undergone fertility-sparing treatment and those who were never diagnosed with endometrial cancer. The researchers also concluded that the higher risks of multiple gestation and cesarean delivery were presumably attributable to the use of artificial reproductive techniques and not the history of endometrial cancer itself.

2. Comparisons of survival between bevacizumab vs. olaparib in platinum-sensitive, relapsed ovarian cancer (KGOG 3052)

The next session was presented by Dr. Se Ik Kim from Seoul National University on the multi-center study KGOG 3052, in which 10 institutions in South Korea had participated. The researchers retrospectively analyzed the survival outcomes of olaparib vs. bevacizumab treatment in patients with relapsed high-grade serous carcinoma of ovary. The included patients were those with BRCA 1/2 mutation (germline or somatic), and who received platinum-based combination chemotherapy for their second-line treatment (platinum-sensitive recurrence). A total of 29 patients who received second-line platinum-based chemotherapy including bevacizumab (Bevacizumab group) and 119 patients who received platinum-based chemotherapy doublets without bevacizumab (Olaparib-intent group) were identified. Among the Olaparib-intent group patients, 83 patients actually received olaparib maintenance after chemotherapy. Multivariate analysis revealed that the Olaparib-intent group had longer progression-free survival (PFS) (adjusted hazard ratio [aHR]=0.566; 95% confidence interval [CI]=0.341–0.940; p-value=0.028) compared to the Bevacizumab group. The overall survival (OS) did not differ between the 2 groups. After conducting propensity score matching for controlling the disease stage, surgical outcomes after the first cytoreductive surgery, treatment-free interval, serum CA-125 levels at first recurrence and surgical outcomes after the second cytoreductive surgery, intention to Olaparib maintenance was still an independent favorable prognostic factor for PFS. As the proportion of olaparib users in the Olaparib-intent group increased, the median PFS further increased while aHR decreased. The authors concluded that intention to olaparib maintenance and actual use of olaparib was associated with significantly better survival outcomes than bevacizumab in second-line treatment of BRCA-mutated, platinum-sensitive, relapsed high-grade serous carcinoma of ovary.

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3. Machine learning-based predictive model for parametrial invasion in patients with early-stage cervical cancer

In the next session, Dr. Kittipat Charoenkwan from Chiang Mai University introduced a computational model for identification of parametrial invasion in women with early-stage cervical cancer. Parametrial invasion of tumor is reported to occur in only 5% to 25% in early-stage cervical cancer [9]. Performing radical hysterectomy may not necessarily yield survival benefits in those women without parametrial tumor invasion. Therefore, accurate prediction of parametrial invasion prior to surgical treatment may prevent the performance of unnecessary aggressive radical hysterectomy. Dr. Charoenkwan and colleagues developed a novel machine learning-based predictive model by analyzing potential clinicopathological risk factors. The authors named iPMI-Econ model that included age, parity, human immunodeficiency virus (HIV) infection status, menopausal status, underlying disease, prior conization, tumor size, stage, and histology, which achieved an area under the curve (AUC) of 0.943. The authors further developed iPMI-Power model that included pelvic lymph node metastasis status and uterine corpus metastasis status in addition to the iPMI-Econ model, which achieved an AUC of 0.972. By developing a relatively simple mathematical model using easily-obtainable clinicopathologic information prior to surgery, the authors were able to build a learning algorithm that may be applied in the clinical settings with good performance to predict parametrial invasion in early-stage cervical cancer.

LUNCHEON SYMPOSIUM

1. Frontline Therapy for newly diagnosed advanced ovarian cancer

In this session, Dr. Bradly Monk from university of Arizona talked about frontline therapy for newly diagnosed advanced ovarian cancer. He began the lecture with the GOG 218 trial of adding bevacizumab with chemotherapy and in the maintenance phase. Dr. Monk explained how they came to design the GOG 218 [10]. The study revealed no survival differences observed with addition of bevacizumab compared chemotherapy alone [10]. Finally, they published it in the *New England Journal* in 2011, and then ultimately got an Food and Drug Administration (FDA) approval in June of 2018. It took seven years after the *New England Journal* publication to get FDA approval because unlike Europe, where they understood the value of PFS, the US regulators felt that OS needed to be the endpoint. Finally, U.S. FDA has accepted PFS is the endpoint for monitoring clinical benefits, but it had to be clinically meaningful and at the minimum had to be 6 months. We can see update in September of 2019 *Journal of Oncology*; there was no survival advantage [11]. BRCA 1/2, homologous recombination repair were not predictors of bevacizumab activity [11]. So, we did chemotherapy first. We did Bevacizumab second, and then we entered the era of PARP inhibitors. Dr. Monk and his colleague have tried to identify biomarkers of PARP sensitivity. They went on to try to identify the beyond-BRCA mutations, which not only included mutations, but epigenetic silencing and promoter methylation, to get the complete picture of who might benefit from a PARP inhibitor. And he said that probably the best assay is myChoice CDx®, because it looks at the genomic scar, the result of the homologous recombination deficiency with the score. He explained that the first thing he wanted you to focus on is BRCA 1, BRCA 2, not the same. Moreover, the molecular signature of BRCA mutation, homologous repair deficiency and homologous repair proficiency is really important when all patients were sensitive to platinum. It is really important to use the biomarker and certainly number of lines of therapy, so the earlier we can integrate these.

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SOLO-1 study revealed that the use of maintenance with olaparib gave a subsequent advantage in regard to PFS with newly diagnosed advanced ovarian cancer and BRCA mutation [12]. He said that SOLO-1 study really changed the flow because we really have not been good at testing the tumor, the somatic mutations, but it changed the workflow. However, he pointed that SOLO-1 was BRCA only, 25% of ovarian cancers. Therefore, they wanted all-comers and they wanted to fix the dosing issue. The result of PRIMA study is that among patients with newly diagnosed advanced staged ovarian cancer with a previous response to platinum, those who received niraparib had better PFS than placebo group, regardless of the status of homologous-recombination deficiency [13]. On April 29th 2020, this was approved by FDA for all-comers. Next, he moved to PAOLA-1 study [14]. He said that PAOLA-1 is a very different study. Number one, it was an investigator-initiated study. And the primary endpoint was all-comers. The HRD endpoint was not an endpoint. The HRD endpoint was not balanced between the arms, and it created a lot of concern about how this is going to be viewed as regulators, but it was sort of submitted at the exact same as PRIMA, and there was no PRIMA arm here. Unlike PRIMA study, where there is an impact in the HR proficient group, there is absolutely no benefit in the homologous recombination proficient benefit of PAOLA-1 [14]. Despite higher discontinuing rate, the FDA approved on May 8th 2020, just 10 days after the April 29th approval of PRIMA. At the end of the session, he showed the Monk algorithm [15] and emphasized that we should do germline testing and probably a panel, and we should also do HRD testing if germline BRCA is wild type.

FOCUSED PLENARY I

1. Immunohistochemical and genetic characteristics of invasive stratified mucin-producing carcinoma of the uterine cervix

The next session was presented by Dr. Eunhyang Park from Yonsei University. Dr. Park introduced invasive stratified mucin-producing carcinoma (ISMC), a recently described entity of human papilloma virus (HPV)-associated endocervical adenocarcinoma. She and her colleagues investigated the immunohistochemical expression of cervical epithelial cell markers, stemness markers, and epithelial-mesenchymal transition (EMT) markers in 10 ISMCs. It was found that ISMC was significantly associated with larger tumor size (p-value=0.011), more frequent lymphovascular invasion and lymph node metastasis (p-value<0.001), higher disease stage (p-value=0.022) and a tendency for worse clinical outcomes (p-value=0.056) compared to other HPV-associated subtypes. ISMC also showed distinct patterns of immunohistochemical properties. It also exhibited frequent STK11, MET, FANCA, and PALB2 mutations compared to the conventional cervical carcinomas, and the genes related to EMT and stemness were frequently altered. The authors concluded that ISMC is an aggressive HPV-associated endocervical adenocarcinoma with stemness and EMT properties and distinct genetic alterations. They also recommended the utilization of PAX8, CK5/6, and p63 as diagnostic triple biomarkers for ISMC based on their analysis on immunohistochemical properties.

2. Circulating tumor cells as a predictive marker for treatment monitoring of ovarian cancer patients

The next session was presented by Dr. Seungmee Lee from Keimyung University on the potential usage of circulating tumor cells as a predictive marker for treatment monitoring of ovarian cancer patients. Dr. Lee prospectively analyzed 49 serial blood samples at multiple time points from 13 women with epithelial ovarian cancer. Dr. Lee and colleagues were able to isolate circulating tumor cells from the blood of ovarian cancer patients with the mean and median count of 20.2 and 6.0 per sample, respectively. During the median follow-up of 22.7

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months, circulating tumor cell count and serum CA-125 levels showed a high concordance with directional change (increasing 71.4% and decreasing 75.0%). When compared to serum CA-125 levels, circulating tumor cell count further demonstrated a significant association with the clinical status of the patients by showing higher sensitivity (100% vs. 60.0%), positive predictive value (55.6% vs. 42.9%), and negative predictive value (100% vs. 87.5%). The authors concluded that circulating tumor cell count was better associated with treatment response and recurrence in comparison to serum CA-125 levels.

3. C-peptide prevents hyperglycemia-induced transglutaminase 2 (TGase2) activation in ovarian cancer cells

Dr. Yung-Taek Ouh of Kangwon National University School of Medicine presented an experimental study on the role of C-peptide in an ovarian cancer cell line. Diabetes mellitus (DM) is a poor prognostic factor in patients with ovarian cancer [16-19]. The increased levels of TGase2 and reactive oxygen species (ROS) found in patients with DM may promote migration and invasion of cancer cells [20,21]. SKOV3 cells were treated with C-peptide, which is deficient in type 1 DM and is known to play an important role in suppressing diabetic complications [22-25], to determine the correlation between TGase2 and ROS. TGase2 was activated by high glucose-induced ovarian cancer by sequential elevation of intracellular Ca^{2+} and ROS levels. C-peptide inhibited high-glucose-induced ROS generation and TGase2 activation. High glucose also promoted the epithelial to mesenchymal transition markers including increased N-cadherin and vimentin, which was prevented by C-peptide. Furthermore, C-peptide inhibited cell migration and invasion induced by high glucose. This study revealed the pathophysiology of ovarian cancer due to hyperglycemia and, in turn, showed that C-peptide may serve as a new treatment for patients with ovarian cancer and DM.

FOCUSED PLENARY II

1. Accuracy of HPV tests using urine samples versus clinician-collected samples for the detection of cervical precancer: a meta-analysis

Dr. Hyun Woong Cho of Korea University College of Medicine published a meta-analysis comparing the accuracy of a human papillomavirus (HPV) test determined using self-collected urine and physician-collected samples to detect pre-cancerous lesions in the cervix. Twenty-one studies were included in the meta-analysis. The HPV test conducted using urine samples was 14%–21% less sensitive for detecting lesions of CIN2 or higher than that conducted using physician-collected samples; there was no difference in specificity. The relative sensitivity was significantly lower in the HPV test conducted using urine samples than that conducted using physician-collected samples; however, there was no difference in the relative specificity. The urine sample-based HPV test using a polymerase chain reaction (PCR)-based assay had comparable sensitivity to the physician-collected sample-based HPV test. Women who refuse or are reluctant to participate in a cervical cancer screening program owing to the COVID-19 pandemic might find that a self-administered urine sample-based HPV test using PCR analysis is an acceptable alternative.

2. Dynamics of fecal microbiota with and without invasive cervical cancer and its application in early diagnosis

Dr. Yoon Hee Lee of Kyungpook National University School of Medicine presented a study examining the correlation between early cervical cancer and the fecal microbiome. The authors also sought to determine if the fecal microbiome could be used as a biomarker using

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machine learning technique. Fecal DNA data were obtained from 17 patients with cervical cancer and 29 healthy controls using 16s rRNA gene sequencing. *Prevotella* was abundant in patients with cervical cancer, while *Clostridium* was abundant in healthy controls. There was a between-group difference in microbiome composition; healthy control women had a more complex symbiotic network than patients with cervical cancer. Through machine learning, seven microorganisms were identified as differentiating factors between the 2 groups; a heat map was deduced that showed the top predictors to be *Prevotella* and *Turicibacter*. The predictive model had good diagnostic value with an AUC greater than 0.9.

3. Concerns regarding the long lead time following a confirmatory test after an abnormal Pap test result in the COVID-19 era

Dr. Miseon Kim of CHA University School of Medicine presented a study that examined the lead time to confirmatory test after abnormal screening Pap test during the COVID-19 era. From January 2019 to December 2020, 1,144 patients with abnormal pap smear results who underwent colposcopy were included in the study. The lead time to colposcopy from the Pap test was examined between 2019 and 2020 was compared. Dr. Kim and colleagues could not determine any difference in the lead time before and after the emergence of COVID-19.

FOCUSED PLENARY III

1. Determining the extent of lymphadenectomy in patients with endometrial cancer

Dr. Wonkyo Shin of the National Cancer Center studied the scope of lymphadenectomy in patients with endometrial cancer. The authors sought to determine if there were clinical factors that could determine the scope of lymphadenectomy or any differences in risk factors depending on the location of lymph node metastases. The study included 468 patients with early endometrial cancer and was conducted from January 2016 to December 2018. Para-aortic lymphadenectomies were performed based on multiple factors, including each patient's preoperative histology, extent of cervical invasion, and cancer grade. Depending on the risk, performance of up to an aortic lymph node resection had a good survival rate. There was no clinical difference relative to the location of the lymph node metastases. This presentation emphasized the importance of risk-group evaluation for determining the scope of lymph node resection in patients with early-staged endometrial cancer.

2. Nomogram for microscopic lymph node metastasis in patients with surgically staged endometrioid endometrial cancer

Dr. Tae-Wook Kong of Ajou University School of Medicine introduced a nomogram that predicted microscopic lymph node metastases. Such metastases are difficult to identify on preoperative imaging of endometrioid endometrial cancer. This study included 338 patients without lymph node metastasis on preoperative imaging who underwent pelvic and para-aortic lymphadenectomy. Of these patients, 9.8% had microscopical lymph node metastases. Nomogram construction included age, CA-125 level, preoperative tumor grade, myometrial invasion on magnetic resonance imaging, cervical stromal invasion, parametrial invasion, and lesion size as variables. The concordance index of the nomogram was 0.860 (95% CI=0.788–0.927), and calibration plots showed a good match between the observed and nomogram-predicted probabilities. This study provides important information to help determine whether to perform lymphadenectomy, as it allows nomogram-based prediction of microscopical lymph node metastases.

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3. Incidence and risk factors of venous thromboembolism (VTE) in patients with cervical cancer using the Korean National Health Insurance data

Dr. Banghyun Lee of Inha University School of Medicine presented a study identifying the incidence rate of VTE and its risk factors in patients with cervical cancer using South Korea's Health Insurance Review and Assessment Service data. Between 2009 and 2018, 49,514 patients with cervical cancer were included. The incidence of VTE was 115 per 10,000 patients. The average age of patients with VTE was 58 years, which was higher than that of patients without VTE. Patients who received chemotherapy as the primary treatment had the highest incidence of VTE; however, the incidence decreased over time. There was a higher frequency of VTE when platinum was included in the chemotherapy, and there was no difference associated with bevacizumab use. Dr. Lee and the chair of this session emphasized that the risk of VTE should be evaluated in patients with cervical cancer and, if necessary, prophylactic treatment should be initiated.

4. Survival analysis of chemoradiotherapy versus only chemotherapy in stage III endometrial cancer: a multicenter study

Dr. Jigeun Yoo of the Catholic University of Korea presented a multicenter retrospective study that compared chemotherapy combined with radiation therapy and chemotherapy alone in stage III endometrial cancer. The study examined OS and toxicity profiles of 80 patients who received 6 cycles each of full-dose chemotherapy and external beam radiation therapy (CRT) and 53 patients who received chemotherapy alone. There was no significant difference in 3-year disease-free survival (DFS), but in IIIc endometrioid histology, the CRT-enforced group showed better 3-year DFS. Grade 4 neutropenia and thrombocytopenia were more frequent in the CRT group.

Distillation session was held at the end of the presentation for the first time at this conference. It provided attendees with an excellent opportunity to organize the background and results of each session and to discuss future directions.

KSGO-KSP JOINT MEETING

1. World Health Organization (WHO) classification of female genital tumors, 5th ed.

Dr. Cheol Lee form of Department of Pathology, Seoul National University Hospital gave a summary of the 5th edition of the WHO classification of female genital tumors that have recently been revised. It was characterized by reflecting molecular pathological classification in addition to the conventional morphological classification. In cervical cancer, HPV infection has established itself as a major axis of classification. HPV independence is rare but has been known to have a poor prognosis. In ovarian cancer, it is worth noting that low-grade serous carcinoma and high-grade serous carcinoma were classified as completely separate diseases with no evidence of transition. In endometrial cancer, carcinosacoma was classified as a carcinoma.

2. European Society of Medical Oncology-European Society of Gynaecological Oncology (ESMO-ESGO) new guideline for endometrial cancer: focusing on molecular classifier

Dr. Han Byul Cho from Yonsei University gave a lecture on the new aspects of ESMO-ESGO classification of endometrial cancer. The molecular classification was attempted in the revised guideline. However, complete molecular classification using whole-genome

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sequencing is difficult to be generalized due to the high cost and inconvenience to use fresh frozen tissue. Therefore, in the newly proposed ProMisE molecular classification, formalin-fixed, paraffin-embedded and immunohistochemical can be used. In the ESMO-ESGO new guideline, the diagnosis algorithm proposed by Vermij and colleagues was adopted, and tumors were classified by three IHC markers (p53, MSH6, PMS2) and somatic mutation analysis of polymerase epsilon [26]. Through this, it is classified into four risk groups: Low/Intermediate/High-intermediate/High.

KSGO-KOSRO JOINT MEETING

1. Adjuvant therapy for postoperative cervical cancer

Dr. Yong Bae Kim from Department of Radiation Oncology, Yonsei University College of Medicine, gave a summary of radiation therapy (RT) for cervical cancer. Concurrent chemoradiotherapy (CCRT) with the addition of cisplatin has been proven in several clinical trials to be an effective cervical cancer treatment. RTOG-0724, which compares the effects of cisplatin and carboplatin/paclitaxel during CCRT in high-risk groups, and GOG-263, which compares RT and CCRT in moderate-risk groups, are ongoing. Surgery is not recommended in most cases for newly revised cervical cancer stage IB3, i.e., 4 cm or larger tumor. In addition, if cancer metastasis is confirmed on the frozen section examination for LN biopsy during surgery, it is better to stop the operation and save the uterus to raise the small bowel at the time of radiotherapy. Also, since it is expected that the function of the ovary will be lost when exposed to 3 grays or more radiation, appropriate judgment is required.

2. Intraoperative detection of lymph node metastasis: hysterectomy or not

Dr. Won Duk Joo from CHA University gave a lecture on the diagnosis of lymph node metastasis during surgery. In cervical cancer, as the International Federation of Gynecology and Obstetrics (FIGO) stage revised in 2018 included lymph node metastasis, the role of resection became important, accordingly, the National Comprehensive Cancer Network guidelines recommend surveillance lymph nodes. To avoid complications, systemic lymphadenectomy is recommended to be performed only when cancer metastasis is detected in the sentinel lymph node using substances such as indigo carmine, indocyanine green (ICG), and technetium (99mTc). According to a trial called ABandoning RAd hyst in cerviX cancer (ABRAX), there was no survival benefit in completing (radical) hysterectomy compared with abandoning surgery when intraoperative metastatic lymph node was detected.

KSGO-KSMO JOINT MEETING

1. Immune checkpoint inhibitors in recurrent gynecologic cancer

Dr. Seung-Hyuk Shim from Konkuk University summarized the role of immune checkpoint inhibitors in recurrent gynecologic cancer. In endometrial cancer, the ratio of deficient mismatch repair and microsatellite instability-high tumor is about 30%, and programmed cell death protein 1 (PD-1) and programmed death ligand 1 (PD-L1) expression are relatively high. Also, tumor-infiltrating lymphocytes are present, which makes it an ideal target for immunotherapy. Thus, the combination of anti-vascular endothelial growth factor along with immuno-oncology has shown promising results. In contrast, recurrent cervical and ovarian cancers have shown disappointing results in several clinical studies. There is an urgent need to discover biomarkers that can select the right patient for the treatment.

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2. Candidate biomarkers for immune checkpoint inhibitors

Dr. Sook-Hee Hong from Department of Internal Medicine, Catholic University gave a presentation on possible biomarker candidates for the immune checkpoint inhibitors (ICIs). Currently, ICIs are not widely used in gynecological cancer, except for endometrial cancer. Gynecological cancer has a low expression of tumor mutational burden and PD-L1, so a more detailed strategy is needed. The T cell-inflamed gene expression profile is also worth considering as a candidate by referring to the case of other carcinomas, but no consensus has been made for the gene mutation that can predict the conditions. Therefore, it is necessary to study the components of the tumor microenvironment and the molecular mechanisms driving these changes, in addition to the existing tumor-focused studies.

TUMOR BOARD

The last session of the meeting consisted of three cases of interactive tumor board review in which three expert panels (Dr. Jae Man Bae from Hanyang University, Dr. Dae Gy Hong from Kyungpook National University, and Dr. Jeong Yeol Park from Ulsan University) discussed possible treatment options with the audience who were able to show their opinions by simultaneous electronic votes.

The first case was a 72-year-old woman with stage IVB high-grade serous carcinoma of the ovary. Opinions regarding the management of the patient were asked sequentially to the audience, and the panels discussed each treatment choice with up-to-date evidence from clinical trials. For this patient, the audience preferred to initiate treatment by diagnostic laparoscopy to determine primary debulking surgery versus neoadjuvant chemotherapy (52% of the audience's choice) in consideration of her old age and advanced disease status. They also wanted to perform tests for germline BRCA and HRD (50% of the audience) at the initial stage of the treatment. The tests resulted in BRCA wildtype and HRD negative. Consequently, the audience chose platinum-based chemotherapy with bevacizumab followed by bevacizumab maintenance (56% of the audience). Unfortunately, the patient recurred after 12 months of platinum-free interval. The recurred lesion was localized in the liver parenchyma on radiology. Most of the audience (60%) chose to perform secondary cytoreduction followed by platinum-based chemotherapy and PARP inhibitor maintenance. Despite the treatment efforts, the patient developed platinum resistance and follow-up tests revealed HRD positive and somatic BRCA mutation. The audience showed the preference of using PARP inhibitors (55%) as her next treatment choice.

The next case was a 67-year-old woman who underwent laparoscopic staging operation and found to have FIGO stage IIIC1 serous carcinoma of the endometrium. The immunohistochemistry revealed p53 abnormality. The audience chose microsatellite instability (MSI) test (46%) as the most helpful test for her optimal treatment followed by human epidermal growth factor receptor 2 (HER2) expression test (28%). The HER2 expression turned out to be weak positive (1+). Despite the weak positivity of HER2 expression, the audience chose the use of trastuzumab in addition to the use of platinum-based chemotherapy (47%). The next frequent choice of treatment was the PORTEC-3 trial regimen (cisplatin with concurrent radiotherapy followed by paclitaxel and carboplatin) (34%).

The last case was a 38-year-old woman with radiologic stage of IB2 squamous cell carcinoma of the cervix. The audience answered that they would perform open radical hysterectomy

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(67%) for the initial treatment. However, the patient underwent laparoscopic radical hysterectomy during which frozen pathology revealed metastatic pelvic lymph nodes. The question was asked to the audience whether to carry on radical hysterectomy. The majority of the audience chose to perform paraaortic lymph node staging and abandon radical hysterectomy for subsequent concurrent chemoradiation therapy (38%). Other opinions included the continuation of laparoscopic radical hysterectomy (29%), discontinuation of radical hysterectomy without paraaortic lymph node staging (24%) and conversion to open radical hysterectomy (9%). The ABRAX study was introduced by Dr. Jae Man Bae which demonstrated similar survival outcomes between those who completed radical hysterectomy and those who abandoned radical hysterectomy after finding pelvic lymph node metastasis intraoperatively [27].

All 3 cases captured the most current issues of each malignant disease and provided an opportunity to review the corresponding evidence from recent clinical trials. The use of PARP inhibitors in advanced epithelial ovarian cancer, utilization of the new molecular classification of endometrial cancer, and the implementation of the results from the laparoscopic approach to cervical cancer (LACC) trial into the clinical setting are all ongoing issues of the current research field. This tumor board session was different from previous conventional format of conference meetings and thereby earned considerable favors from the audience.

AWARDS

The honorable Shin-Poong-Ho-Wol Awards of the 2021 KSGO annual meeting went to Dr. Seung-Hyuk Shim of Konkuk University and Jigeun Yoo of Catholic University for their presentation on *Risk of adverse obstetric outcomes in patients with a history of endometrial cancer: a population-based cohort study* and *Survival analysis of chemoradiotherapy versus chemotherapy alone for stage III endometrial cancer: a multicenter study*, respectively. The same awards for poster presentation were given to Dr. Gwan Hee Han of Kyung Hee University for *Expression of NANOG and AMPK modulate EOC progression through AMPK/mTOR signaling pathway* and Dr. Dan-Ah Chae of Chung-Ang University for *Overexpressed gonadotrophin releasing hormone 2 is a poor prognostic factor of serous ovarian cancer*. Dr. E Sun Paik of Sungkyunkwan University received the Best Paper Award of the Journal of Gynecologic Oncology for his work on *Prediction of survival outcomes in patients with epithelial ovarian cancer using machine learning methods* [28]. Drs. Gun Oh Chong of Kyungpook National University and Chel-Hun Choi of Sungkyunkwan University received the Best Reviewer Awards for their contribution to the journal.

CONCLUSION

The 36th Annual Meeting of the KSGO was the fully virtual meeting organized by the KSGO. This conference made the participants to learn the latest knowledge in various fields in one place.

REFERENCES

1. Sundar SS, Leung E, Khan T, Glasbey J, Abu-Rustum N, Chiva LM, et al. 594 Impact of the covid pandemic on gynaecological cancer surgery – results from the covidsurg gynaecological cancer international study. Int J Gynecol Cancer 2020;30:A123-4.

https://doi.org/10.3802/jgo.2021.32.e75

2. Querleu D, Planchamp F, Chiva L, Fotopoulou C, Barton D, Cibula D, et al. European Society of Gynaecologic Oncology Quality indicators for advanced ovarian cancer surgery. Int J Gynecol Cancer 2016;26:1354-63.
PUBMED | CROSSREF
3. Bhattarai D, Singh S, Jang Y, Hyeon Han S, Lee K, Choi Y. An insight into drug repositioning for the development of novel anti-cancer drugs. Curr Top Med Chem 2016;16:2156-68.
PUBMED | CROSSREF
4. Kobayashi Y, Kashima H, Rahmanto YS, Banno K, Yu Y, Matoba Y, et al. Drug repositioning of mevalonate pathway inhibitors as antitumor agents for ovarian cancer. Oncotarget 2017;8:72147-56.
PUBMED | CROSSREF
5. Kobayashi Y, Kashima H, Wu RC, Jung JG, Kuan JC, Gu J, et al. Mevalonate pathway antagonist suppresses formation of serous tubal intraepithelial carcinoma and ovarian carcinoma in mouse models. Clin Cancer Res 2015;21:4652-62.
PUBMED | CROSSREF
6. Scorilas A, Fotiou S, Tsiambas E, Yotis J, Kotsiandri F, Sameni M, et al. Determination of cathepsin B expression may offer additional prognostic information for ovarian cancer patients. Biol Chem 2002;383:1297-303.
PUBMED | CROSSREF
7. Sun C, Fang Y, Yin J, Chen J, Ju Z, Zhang D, et al. Rational combination therapy with PARP and MEK inhibitors capitalizes on therapeutic liabilities in *RAS* mutant cancers. Sci Transl Med 2017;9:eaal5148.
PUBMED | CROSSREF
8. Sun C, Yin J, Fang Y, Chen J, Jeong KJ, Chen X, et al. BRD4 inhibition is synthetic lethal with PARP inhibitors through the induction of homologous recombination deficiency. Cancer Cell 2018;33:401-416.e8.
PUBMED | CROSSREF
9. Ma C, Zhang Y, Li R, Mao H, Liu P. Risk of parametrial invasion in women with early stage cervical cancer: a meta-analysis. Arch Gynecol Obstet 2018;297:573-80.
PUBMED | CROSSREF
10. Burger RA, Brady MF, Bookman MA, Fleming GF, Monk BJ, Huang H, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med 2011;365:2473-83.
PUBMED | CROSSREF
11. Tewari KS, Burger RA, Enserro D, Norquist BM, Swisher EM, Brady MF, et al. Final overall survival of a randomized trial of bevacizumab for primary treatment of ovarian cancer. J Clin Oncol 2019;37:2317-28.
PUBMED | CROSSREF
12. Moore K, Colombo N, Scambia G, Kim BG, Oaknin A, Friedlander M, et al. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med 2018;379:2495-505.
PUBMED | CROSSREF
13. González-Martín A, Pothuri B, Vergote I, DePont Christensen R, Graybill W, Mirza MR, et al. Niraparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med 2019;381:2391-402.
PUBMED | CROSSREF
14. Ray-Coquard I, Pautier P, Pignata S, Pérol D, González-Martín A, Berger R, et al. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. N Engl J Med 2019;381:2416-28.
PUBMED | CROSSREF
15. Chan JK, Liang SY, Kapp DS, Chan JE, Herzog TJ, Coleman RL, et al. Selecting new upfront regimens for advanced ovarian cancer with biomarker guidance. Gynecol Oncol 2020;159:604-6.
PUBMED | CROSSREF
16. Akhavan S, Ghahghaei-Nezamabadi A, Modaresgilani M, Mousavi AS, Sepidarkish M, Tehranian A, et al. Impact of diabetes mellitus on epithelial ovarian cancer survival. BMC Cancer 2018;18:1246.
PUBMED | CROSSREF
17. Bakhru A, Buckanovich RJ, Griggs JJ. The impact of diabetes on survival in women with ovarian cancer. Gynecol Oncol 2011;121:106-11.
PUBMED | CROSSREF
18. Ferriss JS, Ring K, King ER, Courtney-Brooks M, Duska LR, Taylor PT. Does significant medical comorbidity negate the benefit of up-front cytoreduction in advanced ovarian cancer? Int J Gynecol Cancer 2012;22:762-9.
PUBMED | CROSSREF
19. Minlikeeva AN, Freudenheim JL, Cannioto RA, Szender JB, Eng KH, Modugno F, et al. History of hypertension, heart disease, and diabetes and ovarian cancer patient survival: evidence from the ovarian cancer association consortium. Cancer Causes Control 2017;28:469-86.
PUBMED | CROSSREF

20. Verma A, Guha S, Diagaradjane P, Kunnumakkara AB, Sanguino AM, Lopez-Berestein G, et al. Therapeutic significance of elevated tissue transglutaminase expression in pancreatic cancer. Clin Cancer Res 2008;14:2476-83.
PUBMED | CROSSREF

21. Liou GY, Storz P. Reactive oxygen species in cancer. Free Radic Res 2010;44:479-96.
PUBMED | CROSSREF

22. Bhatt MP, Lim YC, Hwang J, Na S, Kim YM, Ha KS. C-peptide prevents hyperglycemia-induced endothelial apoptosis through inhibition of reactive oxygen species-mediated transglutaminase 2 activation. Diabetes 2013;62:243-53.
PUBMED | CROSSREF

23. Hills CE, Brunskill NJ, Squires PE. C-peptide as a therapeutic tool in diabetic nephropathy. Am J Nephrol 2010;31:389-97.
PUBMED | CROSSREF

24. Calcutt NA, Cooper ME, Kern TS, Schmidt AM. Therapies for hyperglycaemia-induced diabetic complications: from animal models to clinical trials. Nat Rev Drug Discov 2009;8:417-29.
PUBMED | CROSSREF

25. Gubitosi-Klug RADCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: summary and future directions. Diabetes Care 2014;37:44-9.
PUBMED | CROSSREF

26. Vermij L, Smit V, Nout R, Bosse T. Incorporation of molecular characteristics into endometrial cancer management. Histopathology 2020;76:52-63.
PUBMED | CROSSREF

27. Cibula D, Dostalek L, Hillemanns P, Scambia G, Jarkovsky J, Persson J, et al. Completion of radical hysterectomy does not improve survival of patients with cervical cancer and intraoperatively detected lymph node involvement: ABRAX international retrospective cohort study. Eur J Cancer 2021;143:88-100.
PUBMED | CROSSREF

28. Paik ES, Lee JW, Park JY, Kim JH, Kim M, Kim TJ, et al. Prediction of survival outcomes in patients with epithelial ovarian cancer using machine learning methods. J Gynecol Oncol 2019;30:e65.
PUBMED | CROSSREF