Welcome Message

Message from the President of the 1st Congress of Asian Society of Gynecologic Oncology

Dear Colleagues

It is a great honor for us to have an opportunity to host the 1st congress of the Asian Society of Gynecologic Oncology. ASGO has just launched by the grace of the 9 local societies of gynecologic oncology in Asia in order to know each other and cooperate with each other for the purpose of improvement of treatment and prevention of gynecologic cancer.

The 1st congress will provide symposium regarding cervical cancer, because this malignancy must be a leading cause of death in Asia and HPV vaccination is the hot topic for prevention.

On behalf of the local organizing committee, I would like to welcome all the physicians in Asia who are interested in Gynecologic Oncology.



Toshiharu Kamura, MD. Congress President the 1st Biennial Meeting of Asian Society of Gynecologic Oncology Kurume University, Japan



maken by

Soon–Beom Kang, M.D. President, Asian Society of Gynecologic Oncology Seoul National University, Korea

Messages of Congratulations from IGCS, SGO and ESGO



INTERNATIONAL GYNECOLOGIC CANCER SOCIETY

Uniting the Globe

Gynecologic Cancer

in the Fight Against

P0 Box 6387 Louisville, KY 40206, USA adminoffice@igcs.org www.igcs.org

Voice: 1-(502)-891-4575 FAX: 1-(502)-891-4576

November 2, 2009

Soon-Beom Kang, MD, PhD Professor and Chairman Department of Obstetrics & Gynecology Seoul National University College of Medicine 28 Yeongeon-dong Jongno-gu, Seoul 110-744 Korea

Dear Dr. Kang,

On behalf of the International Gynecologic Cancer Society, I would like to extend our hearty congratulations and best wishes on the founding of the Asian Society of Gynecologic Oncology, as well as the inaugural meeting of the ASGO in Tokyo. The officers and members of the IGCS look forward to working with the officers and members of the ASGO to reduce the global burden of women's cancer. We anticipate many opportunities for collaboration between our two societies in professional education, public education, and promotion of research.

I would also like to extend to ASGO members my personal invitation to attend the Thirteenth Biennial Meeting of the IGCS in Prague, the Czech Republic, October 23-26, 2010. Our program chair, Dr. Richard Barakat, and chair of the local organizing committee, Dr. Lucas Rob, are putting together an outstanding academic and social program. We look forward to seeing you there.

Sincerely,

Tonathin S. Bench

Jonathan S. Berek, MD President

J. S. Berek, USA President Elect S. Fujii, Japan Past President I. Vergote, EU Vice President E. Avall-Lundgvist, Sweden Secretary-Treasurer N. Colombo, Italy Secretary-Treasurer-Elect R. R. Barakat, USA

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Council C. L. Creutzberg, Netherlands G. Gitsch, Germany M. Gore, UK W. Gotlieb, Canada S-B. Kang, Korea V. Kesic, Serbia R. J. Kurman, USA K.C. Podratz, USA S. Sagae, Japan



October 30, 2009

Soon-Beom Kang, MD, PhD Professor and Chairman Department of Obstetrics & Gynecology Seoul National University College of Medicine 28 Yeongeon-dong Jongno-gu, Seoul 110-744 Korea

Dear Dr. Kang:

On the happy occasion of the inaugural meeting of the Asian Society of Gynecologic Oncology (ASGO), I convey the greetings of the SGO membership to you and the ASGO members and attendees gathering this November in Tokyo. I also extend my cordial greetings to you and the ASGO governing Council for your leadership in building a regional scientific community to address gynecologic cancers within Asia.

As the new ASGO emerges, SGO stands with you to further gynecologic cancer research, prevention and treatment to women worldwide.

I extend my invitation to dialogue with you and the ASGO leadership in San Francisco, CA in March 2010 during the 2010 SGO Annual Meeting.

Best regards,

Dand Cout

David G. Mutch, MD President, Society of Gynecologic Oncologists

Cc: Daniel Clarke-Pearson, MD – SGO President Elect Mary Eiken – SGO Executive Director



ESGO Council 2009-2011

President Ate G. J. van der Zee, *The Netherlands*

Past President Gerald Gitsch, Germany

President Elect/ Treasurer Nicoletta Colombo, *Italy*

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International Journal of Gynecological Cancer (IJGC) Editor in Chief, Uziel Beller, *Israel*

ENYGO European Network of Young Gynae Oncologists Boris Vranes, *Serbia*

ENGOT European Network of Gynae Oncological Trial Groups Ignace Vergote, *Belgium* Soon-Beom Kang, MD, PhD Professor and Chairman Department of Obstetrics & Gynecology Seoul National University College of Medicine 28 Yeongeon-dong Jongno-gu, Seoul 110-744 Korea

November 3, 2009

Dear Dr. Kang,

On behalf of the Council and members of the European Society of Gynaecological Oncology it is my great pleasure to congratulate you and your colleagues with the founding of the Asian Society of Gynecologic Oncology, as well as with the inaugural meeting of the ASGO in Tokyo.

For ESGO as The voice of Gynaecological Oncology in Europe it is of great importance that another regional scientific community will focus on fighting gynecologic cancers within Asia. We are looking forward to work with ASGO in the future on a global level as our needs and goals in the end are the same; reducing the burden of gynecologic cancer for our patients.

I wish ASGO a bright future and an inspiring and successful first scientific ASGO meeting in Tokyo.

Best regards,

Ate G.J. van der Zee, MD, PhD President

Cc: Nicoletta Colombo – ESGO President-Elect Renata Brandtnerova – ESGO Administrative Office

ESGO Administrative Office

C/o Kenes International | P.O.Box 1726 | 1-3 rue de Chantepoulet | 1211 Geneva 1|Switzerland Tel +41 22 906 9150 |Fax +41 22 732 2607 | Email info@esgo.org | Websites www.esgo.org | www.esgo.forum.org

Meeting Information

Dates and Venue

Dates: November 22 (Sun), 2009 Venue: Toshi Center Hotel 2–4–1 Hirakawa–cho Chiyoda–ku Tokyo 102–0093 Japan TEL: +81 3 3265 8211 FAX: +81 3 3262 1705 http://www.toshicenter.co.jp/e/index.html

Registration

On-site registration is mandatory and registration desk is open at the 7th Floor of the venue: \bigcirc November 21 (Sat), 14:00~17:30 \bigcirc November 22 (Sun), 8:00~17:50

Registration Fee 10,000JPY

*Please note that we accept credit card (VISA, MASTER) or Japanese yen in cash only.

PC Preview

All speakers are requested to bring their presentation data on CD–R or USB memory to PC Preview Desk and upload their presentation data at least 30 min before their session.

PC Preview is open at 7th Floor of the venue: \bigcirc November 22 (Sun), 8:00~15:30

PC environment for presentations

Accepted application format: Windows PowerPoint 2003/2007 Accepted media: CD–R (CD–RW will not accepted), USB memory or PC

Notes:

1) If you use your own PC, please bring a special adaptor by your own.

- 2) If you would like to use presentation data with Macintosh and/or moving images, please bring your own PC.
- 3) In the file name, please include the presentation number and presenter's name.
- 4) Other versions may cause trouble with layouts and make characters unreadable. Please avoid using special characters for the same reason.
- 5) Recommended typeface: Century, Century Gothic, Arial, Times New Roman
- 6) If some data are linked to PowerPoint data, such as still images, moving images and charts, save all the linked data and check that data function properly beforehand.
- 7) Please conduct PC operation tests in advance to ensure that your data work properly even in PCs other than the one you used to create the data.

Poster View & Tour

Date:

Display	8:00~10:00, November 22 (Sun)
Poster Tour	14:00~15:30, November 22 (Sun)
Remove	17:00~18:00, November 22 (Sun)

Venue: Room 705 and Room 706 (7th Floor)

Notes for Poster view & Tour

- 1) All posters are to be written entirely in English.
- 2) A presentation number to be placed at the top left of the poster will be provided by the Secretariat. Each author is requested to indicate "the title" "the authors' names" and "the authors' affiliations" at the top right of the panel within an area measuring 70 cm wide by 20 cm high.
- 3) The usable area of the contents is the size measuring 90 cm wide by 180 cm high. The layout of the presentation contents is at the authors' discretion.
- 4) Posters are attached to the boards with thumbtacks, which will be provided by the Secretariat. No paste, glue, staples or nails are permitted.
- 5) Please stop by Poster Reception in front of Room 706.
- 6) Please stay in front of your poster during Poster Tour.



Correspondence

Secretariat of the 1st Biennial Meeting of ASGO c/o MA Convention Consulting Dai 2 Izumi-shoji Bldg., 4-2-6 Kojimachi, Chiyoda-ku, Tokyo 102-0083 JAPAN Phone: +81 3 5275 1191 Fax: +81 3 5275 1192 E-mail: asgo2009@macc.jp

Access to Venues



Access to the Toshi Center Hotel

- 4 minute-walk from Exit No.1 of Kojimachi station, Yurakucho Subway Line.
- · 4 minute-walk from Exit No.4 or 5 of Nagatacho Station, Yurakucho / Hanzomon Subway Lines.
- · 3 minute-walk from Exit No.9 of Nagatacho Station, Nanboku Subway Line.
- · 8 minute-walk from Exit D of Akasaka Mitsuke Station, Marunouchi / Ginza Subway Lines.
- · 14 minute-walk from Kojimachi exit of Yotsuya Station, JR Chuo Line.
- \cdot By bus, Hirakawacho 2–chome Toshi Center–mae.
 - (Shinbashi Ichigaya Kotakibashi Shako route)
- \cdot By car, five minutes from kasumigaseki exit, Shuto Expressway.









Scientific Meeting Program

November 21 (Sat) Council Meeting

November 22 (Sun) Scientific Meeting

	Room 701	Room 705-706
9:00	8:50-9:00 Opening Address	9.00-
	Symposium on Cervical Cancer	Poster View
	Part 1 "Epidemiology and Diagnosis"	
	Chairpersons: Mohammad Farid Aziz(Indonesia) Ikuo Konishi (Japan)	
10:00	Speakers: Woong Ju (Korea)	
	Annie NY Cheung (Hong Kong) Heru Priyanto Samadi (Indonesia)	
	Chih Long Chang (Taiwan)	
11.00	Symposium on Cervical Cancer	
11.00	Part 2 "HPV Vaccine and Prevention" sponsored by GSK	
	Hiroyuki Yoshikawa(Japan)	
	Speakers: Hyun Hoon Chung (Korea) Ryo Konno (Japan)	
12:00	Supriadi Gandamiharja (Indonesia)	
	12:00-12:40 Lunch Time	
	12:40-13:40	
13:00	Commemoration Lecture from IGCS and SGO	
	Speaker: Edward L. Trimble (National Cancer Institute, United States)	
14.00		13:40-15:10 Poster Tours
14:00		
15:00		
	15:10-17:10	
	Symposium on Cervical Cancer	
	Chairpersons: Sarikapan Wilailak (Thailand)	
16:00	Satoru Sagae (Japan)	
	Kung Liahng Wang (Taiwan)	
	Hiroaki Kobayashi (Japan) Chomporn Sitathapee (Thailand)	
17.00	Shyam Kishore (India)	
17.00	Chia Yin Nin (Singapore)	
18:00		
	18:15-20:00	
	Gala Dinner at Grand Prince Hotel Akasaka	
	(47th Annual Meeting of JSGO & 32nd Annual Meeting of JSGOS)	
19:00		
20:00		

Program



Lecture Program

Opening Address

Date and Time: November 22nd (Sunday) 8:50~ Session Room: Room 701 Soon Beom Kang Toshiharu Kamura

Closing Address

Date and Time:	November 22nd (Sunday) 17:30~
Session Room:	Room 701
	Toshiharu Kamura

Commemoration Lecture from IGCS and SGO

Date and Time:November 22nd (Sunday) 12:40~13:40Session Room:Room 701

Global cooperation in gynecologic cancer

Chair:Shingo Fujii (National Hospital Organaization Kyoto Medical Center, Japan)Speaker:Edward L. Trimble (National Cancer Institute, USA)

Symposium on Cervical Cancer

Part 1 Epidemiology and Diagnosis

Date and Time: November 22nd (Sunday) 9:00~10:40 Session Room: Room 701

Chairs: Mohammad Farid Aziz (University of Indonesia, Indonesia) Ikuo Konishi (Kyoto University, Japan)

1. Risk factors of Gynecologic Cancer

Woong Ju (Department of Obstetrics and Gynecology, School of Medicine, Ewha Womans University, Seoul, Korea)

2. Epidemiology and Screening of Cervical Cancer in Hong Kong

Annie NY Cheung (Department of Pathology and Department of Obstetrics and Gynaecology, The University of Hong Kong, Hong Kong)

3. Prognostic significance of Serum Vascular Endothelial Growth Factor-C (Serum VEGF-C) and Lymph-Vascular Space Invasion in Early Stage Cervical Cancer

Heru Priyanto Samadi (Oncology Division – Department of Obstetrics and Gynecology. Dr. Moewardi Hospital Faculty of Medicine Sebelas Maret University –. Solo. Centre Java. Indonesia) 4. Tumor Necrosis Factor-alpha Promoter Polymorphisms in Neuroendocrine Adenocarcinoma of the Uterine Cervix

Chih Long Chang (Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei Taiwan)

Part 2 HPV Vaccine and Prevention sponsored by Glaxo Smith Kline

Date and Time: November 22nd (Sunday) 10:40~12:00 Session Room: Room 701

- Chairs: Hee Sug Ryu (Ajou University, Korea) Hiroyuki Yoshikawa (University of Tsukuda, Japan)
- 1. Current status of HPV infection and vaccination in Korea Hyun Hoon Chung (Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea)
- Efficacy, Immunogenicity and Safety of HPV-16/18 AS04 Adjuvanted Vaccine and Evaluation of Cost-Effectiveness in Japan

Ryo Konno (Department of Obstetrics and Gynecology, Jichi Medical University, Saitama Medical Center, Saitama, Japan)

3. Celecoxib as a future chemoprevention agent by reduces proliferation, increases apoptosis and tumor size reduction through Cox-2-PGE2 pathway activity

Supriadi Gandamihardja (University of Padjadjaran, Bandung, Indonesia)

Part 3 New Trend of Treatment

Date and Time: November 22nd (Sunday) 15:10~17:30 Session Room: Room 701

Chairs: Sarikapan Wilailak (Ramathibodi Hospital, Mahidol University, Thailand) Satoru Sagae (JR Sapporo Hospital, Japan)

1. Laparoscopic management of cervical cancer

Joo–Hyun Nam (Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea)

2. Laparoscopic Extraperitoneal Para-aortic Lymph Node Dissection in Gynecologic Cancers

Kung Liahng Wang (Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan)

3. Abdominal radical trachelectomy for invasive cervical cancer patients who desire preserving fertility Hiroaki Kobayashi (Dept. of Gynecology and Obstetrics, Graduate School of Medical Scineces, Kyushu University, Fukuoka, Japan)

4. Evolving Radiotherapy in Cervical Cancer; from 2D to 4D-IGRT

Chomporn Sitathanee (Radiation Oncology Division, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand)

5-1. Are we justified for concomitant chemo-radiation in Advanced Stage Cancer Cervix? Shyam Kishore Shrivastava (Department of Radiation Oncology, Tata Memorial Hospital,

Parel, Mumbai, India)

5-2. An audit of Phase II Randomized Trial Comparing Intensity Modulated radiation Therapy (IMRT) with Conventional Radiation Therapy in Stage IIB Carcinoma Cervix

Shyam Kishore Shrivastava (Tata Memorial Hospital, Parel, Mumbai, India)

6. New Trends of Treatment for Cervical Cancer: The Singapore Experience: the use of the GOG score to tailor postop management for early stage cervical cancer

Chia Yin Nin (Department of Gynaecologic Oncology, KK Women's and Children's Hospital, Singapore)

	November 22nd (Sur	nday) Room 705-706
9:00~	~ Poster View 13:40~15:10	Poster Tours
P-01	Follow-up Date of patients with patients w Eunseop Song (Inha University Hospita	vith LSIL I, Incheon, Korea)
P-02	Nestin Expression in Cervical Intraepithel Jae Yun Song (Department of Obstetric Medicine, Seoul, Korea)	al Neoplasia and Cervical Cancer s and Gynecology, Korea University College of
P-03	A predictor for treatment failure after loop cervix	electrosurgical procedure of CIN to CIS of the uterine
	Science, Inchon, Repu	blic of Korea)
P-04	Risk factors of recurrence for high grade c vaporization Kouichiro Kawano (Kurume University	ervical intraepithelial neoplasia after carboxydioxide
P-05	Human Papillomavirus (HPV) L1 Capsid F Cervical Intraepithelial Neoplasia 1	Protein and HPV Type 16 as Prognostic Markers in
	Young Sam Choi (Department of Obste Medical School, Gwan	trics and Gynecology, Chonnam National University gju, Korea)
P-06	Intention to Obtain Human Papillomavirus Women	Vaccination among Taiwanese Undergraduate
	Ya-Min Cheng (Department of Obstetr Cheng Kung University	ics and Gynecology, College of Medicine, National 7, Tainan, Taiwan)
P-07	Cost-effectiveness Analysis of HPV vacc Raoh-Fang Pwu (School of Health Care	i nation in Taiwan Administration, Taipei Medical University, Taipei,
P-08	Human papillomavirus infection and cervi cohort-study	cal neoplasia in Taiwan: A long-term follow-up
P-09	Hui-Chi Chen (Genomics Research Cen Evaluation of Signal Pattern of High-Risk	ter, Academia Sinica, Taipei) Human Papillomavirus in Thin-Layer Cervical
	Chih-Ming Ho (Gynecologic Cancer Cer Cathay General Hospita	n Situ Hydridization Assays hter, Department of Obstetrics and Gynecology, 1. Taipei, Taiwan)
P-10	Immunoglobulin A secretion in saliva indu Yong Wook Jung (Department of Obste Medicine Seoul Kore	ced by AS04-adjuvanted HPV-16/18 vaccine trics and Gynecology, Yonsei University College of ca)
P-11	Outcomes of human papillomavirus infect	ion according to the genotypes
P-12	Evaluation and comparison of HPV genoty and DNA sequencing method	pes in cervical lesions by the microbead-based array
P-13	Young Lae Cho (Kyungpook National U Study for early cervical neoplasia confirm Hong-Bao Kim (Collage of Madicing Ho	niversity Hospital, Daegu, Korea) ed by cervical conization
P-14	Conservative management for stage la1 so positive resection margin after conization	quamous cell carcinomas of the uterine cervix with
	Woo Young Kim (Ajou University Scho	ol of Medicine, Suwon, Korea)

 Mi-Kyung Kim (Department of Obstetrics and Gynecology, Seoul National University, College of Medicine, Scoul, Korea) P-16 Laparoscopic radical trachelectomy in young women with early cervical cancer Joo-Hyun Nam (Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Scoul, Korea) P-17 Fertility Preservation by Photodynamic Therapy in Early Cervical cancer or Endometrial Cancer Chan Lee (Comprehensive Gynecology Cancer Center, Bundang CHA General Hospital, College of Medicine, CHA University, Seongnam, Korea) P-18 Characteristics and Orgonosis of cervical cancer in young women Hei-Yu Lau (Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, National Yang-Ming University, Taipei, Taiwan) P-19 Iaparoscopic surgical staging for locally advanced cervical carcinoma: comparison with primary concurrent chemoradiation Dae Gy Hong (Department of Obstetrics and Gynecology, Kyungpook National University Graduate School of Medicine, Daegu, Korea) P-20 Urological evaluation after nerve sparing radical hysterectomy Chung Won Lee (Department of Obstetrics and Gynecology, Soul St. Mary hospital, Seoul, Korea) P-21 Analysis of risk factors for parametrial involvement and the need for parametrial resection in early stage cervical cancer Joong-Yeol Park (Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea) P-22 Influence of post operative adjuvant concurrent chemo radiation on survival for high-risk early stage cervical cancer—K hospital experience Rama P Namuduri (Department of Gynecological Oncology, KW Women's and Children's Hospital, Singapore) P-23 The Role of Celecoxib in Cox-2-PGE2 pathways activity, proliferation, apoptosis and tumor size reduction on concurrent chemotherapy and radiation therapy for cervical cancer Supriadi Gandamihardja (University of Padjadj	P-15	Feasibility of conservative management for stage IB1 cervical cancer with invasion depth of less than 5mm (microinvasive carcinoma)
 P-16 Laparoscopic radical trachelectomy in young women with early cervical cancer Joo-Hyun Nam (Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Scoul, Korea) P-17 Fertility Preservation by Photodynamic Therapy in Early Cervical cancer or Endometrial Cancer Chan Lee (Comprehensive Gynecology Cancer Center, Bundang CHA General Hospital, College of Medicine, CHA University, Seongnam, Korea) P-18 Characteristics and prognosis of cervical cancer in young women Hei-Yu Lau (Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, National Yang-Ming University, Taipei, Taiwan) P-19 Iaparoscopic surgical staging for locally advanced cervical carcinoma: comparison with primary concurrent chemoradiation Dae Gy Hong (Department of Obstetrics and Gynecology, Kyungpook National University Graduate School of Medicine, Daegu, Korea) P-20 Urological evaluation after nerve sparing radical hysterectomy Chung Won Lee (Department of Obstetrics and Gynecology, Scoul St. Mary hospital, Seoul, Korea) P-21 Analysis of risk factors for parametrial involvement and the need for parametrial resection in early stage cervical cancer Jeong-Yeol Park (Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea) P-22 Influence of post operative adjuvant concurrent chemo radiation on survival for high-risk early stage cervical cancer – KK hospital experience Rama P Namuduri (Department of Gynecology, KK Women's and Children's Ilospital, Singapore) P-23 The Role of Celecoxib in Cox-2-PGE2 pathways activity, proliferation, apoptosis and tumor size reduction on concurrent chemotherapy and radiation therapy for cervical cancer Supriadi Gandamihardja (University of Padjadjaran, Bandung, Indonesia) P-24 Cisplatin and etoposide as neoadjuvant chemotherapy in patients with stages IIB-IIIB cervical cancer: A Phase II study Yoon Young Hwang (Compr		Mi-Kyung Kim (Department of Obstetrics and Gynecology, Seoul National University, College of Medicine, Seoul Korea)
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Medical Center, Seoul, Korea		Medical Center, Seoul, Korea)

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P-28	Cervical Cancer Prevention in Developing Country
	See and Treat Model (Jakarta-Indonesian Perspective)
	Laila Nuranna (Department of Obstetrics and Gynecology, Faculty of Medicine, University of
	Indonesia Jakarta, Indonesia)
P-29	Evidence-Based Performance Measures of Cervical Cancer Care Quality in Taiwan
	Mei-Shu Lai (Institute of Preventive Medicine, College of Public Health, National Taiwan
	University, Taipei, Taiwan)
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Global cooperation in gynecologic cancer

Edward L. Trimble, MD, MPH

National Cancer Institute, USA

In many areas, the progress we have made by working together against gynecologic cancer is clear. Let us start with gestational trophoblastic disease, for example. This was one of the first cancers in which chemotherapy was shown to be active. Now, we are able to treat and cure almost all women with gestational trophoblastic disease with a combination of surgery and chemotherapy. Next let us turn to cervical cancer. We developed both surgical and radiation treatment for cervical cancer more than 100 years ago. Today, we can prevent the transmission of HPV infection with prophylactic vaccines, we can screen for precancerous changes with Pap smears, and we have effective treatment for CIN 3 up to locally advanced cervical cancer. Nonetheless, the global incidence and mortality from cervical cancer reminds us that we have much work to do in order to decrease the incidence and the mortality from cervical cancer. For ovarian and endometrial cancer, we have made major strides with both surgery and chemotherapy. Recent discoveries in molecular biology of these diseases have helped us develop targeted therapies for the different subtypes of ovarian cancer.

One key area on which we need to continue to work together is education, both professional and public. We need to ensure that we train gynecologic oncologists who can perform the best possible surgery for women with gynecologic cancer, as well as coordinate their care with other medical disciplines. We need to ensure that we train gynecologic pathologists who are familiar with the various subtypes of gynecologic cancer and their clinical implications. We need to train medical oncologists and radiation oncologists who have expertise in the treatment of gynecologic cancer and who can work closely with gynecologic oncologists. There are many other disciplines which need to be involved as well, including nursing, pharmacy, biostatistics, epidemiology, psychology, and palliative medicine. Only through close multidisciplinary collaboration in treatment, translation research, and clinical trials can we continue to make progress in gynecologic cancer

We also need to work together to educate the public about gynecologic cancer. Important educational messages include the benefits of a healthy lifestyle, regular cancer screening and prevention efforts, early symptoms of gynecologic cancer, and the importance of basic, translational, and clinical research. We also need to work together to educate our policy makers about how best to prevent cancer, to screen for cancer, and to deliver the optimal multidisciplinary care for women with cancer.

On behalf of the International Gynecologic Cancer Society, the Society of Gynecologic Oncologists, and the European Society of Gynecologic Oncology, I congratulate the Asian Society of Gynecologic Oncology on its founding and its inaugural biennial meeting. Through the effective collaboration of our four sister societies, we can do much to reduce the global burden of gynecologic cancer among women.

Risk factors of Gynecologic Cancer

Woong Ju, M.D.^{1,2}

Department of Obstetrics and Gynecology, School of Medicine, Ewha Womans University, Seoul, Republic of Korea¹, Medical Research Institute, School of Medicine, Ewha Womans University, Seoul, Korea²

Human papillomavirus (HPV) infection plays a central etiologic role in development of cervical cancer. Although HPV is a necessary cause of cervical cancer, not all people with HPV infection suffer from cervical cancer, indicating the role of cofactors. Factors investigated regarding the association with persistent HPV infection include host genetic polymorphism, smoking, sexual behavior, lifestyle, socioeconomic status. Some epidemiologic studies have reported association between those cofactors and development of cervical cancer. Further study elucidating cofactors of cervical cancer is in need.

Among gynecological cancers, endometrial cancer and ovarian cancer, the so called endocrine-related cancers, are known to be affected by hormonal and reproductive events. The risk factors for endometrial cancer include nulliparity, early menarche, late menopause, obesity, and postmenopausal estrogen replacement therapy. Although the etiology of ovarian cancer has not been determined, higher parity and oral contraceptive use have been reported to reduce the risk of ovarian cancer. Recently phytoestrogens came into interest because plant-derived compounds possessing estrogen activity have been reported to be related inversely to the risk of endometrial cancer or ovarian cancer.

Large scale clinical trials investigating the chemoprevention effect of dietary ingredients are warranted.

Epidemiology and Screening of Cervical Cancer in Hong Kong

Annie NY Cheung¹, Hextan YS NGAN²

Department of Pathology and Department of Obstetrics and Gynaecology, The University of Hong Kong¹, Queen Mary Hospital, Hong Kong²

Worldwide, cervical cancer is the second most common cancer in women. In Hong Kong, cervical cancer was the fifth most common cancer in females in 2006. The crude and age-standardised incidence rate was 12.8 and 9.4 per 100 000 female population. Cervical cancer was the eighth most common cause of female cancer registered deaths in 2007 with a crude and age-standardised mortality rate was 3.5 and 2.3 per 100 000 standard population.

Despite of the advanced socioeconomic development with some of the best basic health indices in the world, screening for cervical cancer has been carried out in Hong Kong in a predominantly opportunistic fashion when cervical cytology became available in Hong Kong in the 1960s. Nevertheless, a steady decline in the overall age adjusted incidence decreased from 24.9 in 1972–74 to 9.5 per 100,000 in 1999–2001, corresponding to an average annual reduction of 4.0% in these three decades.

The Cervical Screening Programme of Department of Health was launched in 2004. This government operated programme educates women to attend cervical cancer screening and provides a prospective record and recall function for those who have received cytology screening. Their smears can be taken at public or private sectors on a self-financed basis. The programme also encourages accreditation of smear takers, colposcopists and cervical cytology reporting laboratory. Professional guidelines on organization of cervical cytology laboratory and management of abnormal cervical cytology have been established.

In Hong Kong, most laboratories adopt the Bethesda System for reporting of cervical cytology. Liquid based cytology constitutes to a large proportion of the practice. HPV DNA testing is increasingly used mainly for triage of women with ASC–US. Clinical history, physical examination, colposcopy and biopsies are implicated for management of abnormal cervical smear.

The two prophylactic cervical cancer vaccines, protecting against HPV types 16 and 18, have been registered in Hong Kong. Continued education of the public on cervical cancer prevention, human papilloma virus and its vaccine as well as the importance of continued cervical cancer screening is important for further reduction in incidence of cervical cancer.

Prognostic significance of Serum Vascular Endothelial Growth Factor-C (Serum VEGF-C) and Lymph-Vascular Space Invasion in Early Stage Cervical Cancer

Heru Priyanto Samadi, MD¹, Andrijono, MD², M.F Azis, MD²

Oncology Division – Department of Obstetrics and Gynecology. Dr. Moewardi Hospital Faculty of Medicine Sebelas Maret University –. Solo. Centre Java. Indonesia¹, Oncology Division – Department of Obstetrics and Gynecology. Dr. Cipto Mangunkusumo Hospital. Faculty of Medicine University of Indonesia – Jakarta. Indonesia²

Background

The management of early stage cervical cancer still challenging. Several clinico-pathological prognostic factor:stage, bulky tumor, stromal deep invasion, differentiation, histology, lymph vascular space invasion and status of lymph-node recently use on clinical practice. Several bio-molecular prognostic factors still on research.

Vascular endothelial growth factor (VEGF) and VEGF-C play a crucial role in the regulation of tumor growth and metastasis. The current study examined the significance of serum VEGF and VEGF-C levels in relation to conventional clinicopathologic parameters, response to treatment, and survival in patients with cervical carcinoma.

Serum Vascular Endothelial Growth Factor–C(VEGF–C), as an angiogenic and lymphangiogenic factor have an important role in metastasis. Can we use it as prognostic factors in early stage cervical cancer.

Purpose of the study:

The aim of the study was to investigate prognostic value of Serum Vascular Endothelial Growth Factor-C (Serum VEGF-C) and lymph-vascular space invasion as a predictor to lymph node metastasis in early stage cervical cancer.

Method(s):

Fourteen seven consecutive patients with early-stage cervical cancer on January-October 2007 included in this case control study. 14 patient with lymph node metastasis as cases and 33 patient without it as control. 5 ml blood examined preoperatively by ELISA method to determined Serum VEGF-C levels.

Result(s):

Cut-off point serum VEGF-C levels in this study was 10.066 pg/ml, with 78,57% sensitivity and 96,97% specificity. Lymph node metastasis patient with serum VEGF-C level>10.066 pg/ml increase by OR 80, 95% CI 7,99;800,71 and p=0,000. Lymph node metastasis patient with lymph vascular space invasion increase by OR 20, 95% CI 2,32;171,77 and p=0,006. Lymph vascular space invasion increase by OR 12,5, 95 % CI 1,44; 108,18 and p=0,022 in patient with VEGF-C Level>10.066 pg/ml. Multivariate analysis conclude serum VEGF-C can be use as independent prognostic factor on lymph-node metastasis.

Conclusion(s):

Serum VEGF-C is potential bio-marker as prognostic factor to lymph node metastasis in early stage cervical cancer.

Tumor Necrosis Factor-alpha Promoter Polymorphisms in Neuroendocrine Adenocarcinoma of the Uterine Cervix

Chih Long Chang, MD, PhD¹, TC. Chang, MD², YM. Shien, MD³, KL. Wang, MD¹

Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei Taiwan¹, Department of Obstetrics and Gynecology, Chang–Gung Memorial Hospital, Tao–Yuan Taiwan², Department of Obstetrics and Gynecology, Veterans General Hospital, Taipei Taiwan³

<u>Purpose of the study</u>:

The present study describes a large series of neuroendocrine cervical carcinoma (NECC) diseases, regarding the diagnosis, treatment, HPV status and prognosis in a multi-institutional based analysis in Taiwan. We investigate the gene promoter polymorphism of tissue necrosis factor alpha($\text{TNF}\alpha$), one of the immune-associated cytokine in this rare disease and compare with those in squamous cell carcinoma of uterine cervix.

Method(s):

Clinical data of 102 cases with NECC were collected and reviewed. DNA was extracted from their paraffinized tissues after dissecting out of tumor parts. HPV typing was determined by polymerase chain reaction (PCR) with L1 consensus primers and direct sequencing. TNF α gene promoter polymorphism (-308 and -1031) was performed by PCR with designed primers and restriction fragment length polymorphism (RFLP).

Result(s):

Survival analysis shows about 1/3 of NECC patients had relatively long-term survival. Our data provide evidence for TNF α promoter polymorphisms over -308 and -1031 regions in neuroendocrine adenocarcinoma of cervix comparing to squamous cell typed cervical cancer.

Conclusion(s):

TNF α is a pro-inflammatory cytokine, and evidences implicated that TNF α in inflammation microenvironment might enhance tumorigenesis. Its production could be influenced by promoter gene polymorphisms, and therefore TNF α promoter polymorphisms might play a role in the pathogenesis or the actual biological behavior *in vivo* in NECC.

Current status of HPV infection and vaccination in Korea

Hyun Hoon Chung, MD, Jae Weon Kim, MD, Noh-Hyun Park, MD, Yong-Sang Song, MD, Soon-Beom Kang, MD

Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea

Cervical cancer is an important cause of cancer-related deaths in women in developing countries. In Korea, cervical cancer is the third leading cancer among females and is fifth highest in mortality. The persistent oncogenic human papillomavirus (HPV) infections are the greatest risk of developing cervical intraepithelial neoplasm and invasive cancer. The overall prevalence of HPV was 10.4% in Korea and strong risk factors for HPV infection included a young age at sexual debut. The National Cancer Screening Program, which includes cervical cancer screening, has the following principles: the main screening tool is the Papanicolaou test conducted by gynecologists, which targets all women age 30 and over, and which is done every 2 years. HPV DNA tests have not yet been permitted as a screening test for cervical cancer in Korea; however, these are conducted along with a Pap test for screening cervical cancer in the clinic. The use of prophylactic HPV vaccine has been accepted in Korea; The Korean Society of Gynecologic Oncology and Colposcopy's recommendation for routine vaccination is for females aged 15-17 years with a catch-up vaccination recommended for females aged 18-26 years who have not been previously vaccinated. However, many people in Korea are not familiar with the HPV vaccine. Therefore, it is necessary to improve awareness for the disease and HPV vaccination and to establish the effective strategies to obtain funding for HPV vaccination. In the future, cervical cancer is expected to disappear throughout the world through a combination of vaccination and qualified screening programs for cervical cancer.

Efficacy, Immunogenicity and Safety of HPV-16/18 AS04 Adjuvanted Vaccine and Evaluation of Cost-Effectiveness in Japan

Ryo Konno¹, Hiroyuki Yoshikawa²

Department of Obstetrics and Gynecology, Jichi Medical University, Saitama Medical Center, Saitama, Japan¹, Department of Obstetrics and Gynecology, Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Japan²

We report final results on the immunogenicity and safety at month 24 of the phase II double-blind randomized controlled study with HPV-16/18 AS04-adjuvanted vaccine, conducted in healthy women aged 20–25 years in Japan. The primary objective of this study was to demonstrate the efficacy of the vaccine against persistent infection (6-month definition) associated with HPV-16/18 in women who were seronegative at Month 0 and DNA negative at Month 0 and Month 6 for the corresponding HPV type. Secondary objectives included immunogenicity and safety (up to 24 months). A total of 1,040 healthy women aged 20–25 years were vaccinated;519 women in the HPV group (HPV) and 521 women in the hepatitis A control group (HAV) between April and October 2006. Vaccine efficacy was analysed in the according to protocol cohort for efficacy (ATP-E=1002; HPV=501, HAV=501). Vaccine efficacy against persistent infection (6-month definition) with HPV-16/18 was 100% [95.5% CI: 71.3, 100, p<0.0001], with no case in the HPV group versus 15 cases in the HAV group. All HPV vaccine recipients were still seropositive at Month 24, with sustained antibody response. Vaccine safety was similar in both treatment groups. In the study population of 20–25 year old Japanese females, the HPV-16/18 vaccine showed 100% protection against persistent infection with HPV-16/18 (6-month definition), high immune response and a favorable safety profile.

Furthermore, to estimate the clinical and economic impact of implementing HPV vaccination in Japan, focusing on morbidity, mortality and cost effectiveness from the societal and healthcare provider's perspectives. HPV vaccination was expected to reduce the disease burden by reducing the incidence of cervical cancer cases and cervical cancer deaths by approximately 73 % over lifetime. With a vaccine cost at 36,000 yen/course, it was estimated that HPV vaccination of all 12-yr-old girls would save Japanese society about 19 billion yen. From the healthcare perspective, the incremental cost-effectiveness ratio of vaccinating a single cohort of 10 to 45-yr-old multi cohort yielded 370,620 yen per quality-adjusted life year (QALY) gained. HPV vaccination of Japanese women is predicted to be a very cost effective way to reduce cervical cancer morbidity and mortality compared with the current situation.

Celecoxib as a future chemoprevention agent by reduces proliferation, increases apoptosis and tumor size reduction through Cox-2-PGE2 pathway activity

Supriadi Gandamihardja, MD¹, Firman F Wirakusumah, MD¹, Herri Sastramihardja, MD¹, M Nurhalim Shahib, MD¹, M Farid Aziz, MD²

University of Padjadjaran, Bandung, Indonesia¹, University of Indonesia, Jakarta, Indonesia²

Purpose of study: Cervical cancer is the second most common cancer in developing countries which can be reduced by HPV vaccines, screening programs and chemoprevention. But most research should be performed to find a good chemoprevention agent. Selective COX-2 inhibitor, Celecoxib, has a significant effect for increasing apoptosis, reducing proliferation and tumor growth on experimental study, no research has been done to examine these changes in human cervix. The effect of Celecoxib on cervical cancer and its pathogenesis can be used as a basis for conducting trials on precancer lesion with Celecoxib as a chemoprevention agent.

Method: A prospective study with pretest-posttest controlled group design was done in 2008 at the Hasan Sadikin Hospital Bandung by recruiting 20 cervical cancer patients who received Celecoxib and CT-RT, and another controlled group of 21 patients treated by CT-RT only. Cervical tissues obtained by biopsy were sent for mRNA COX-2 assessment by RT-PCR and COX-2 enzyme, Ki-67, and Caspase-3 as proliferation and apoptosis markers, assessed by immunohistochemistry. Cervical tumor size was measured by transabdominal ultrasonography. All variables were obtained before and after external CT-RT. Data were analyzed by using Wilcoxon test and Pearson's correlation test.

Result: The results showed a significant effects of selective COX-2 inhibitor to synchronized reduction of mRNA COX-2 and COX-2 enzyme expression level (p<0.01), which represented COX-2-PGE₂ pathways inhibition, reduce Ki-67 expression level (p<0.01), increase Caspase-3 expression level (p<0.01) and tumor size reduction (p<0.01). There were significant correlations between COX-2 enzyme expression level and mRNA COX-2, Ki-67 and Caspase-3 expression level changes and tumor size reduction.

Conclusion: Celecoxib plays a significant role in reducing tumor size based upon COX-2-PGE₂ pathways activity, which reduces proliferation and increases apoptosis and might act as chemoprevention agent.

Keywords: Celecoxib, mRNA-COX-2, COX-2 enzyme, proliferation, apoptosis, tumor size reduction, chemoprevention.

Laparoscopic management of cervical cancer

Joo-Hyun Nam, MD, PhD

Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea

Purpose of the study: The aim of this study was to compare the surgical and survival outcomes of patients treated by type III laparoscopic radical hysterectomy (LRH) with lymphadenectomy and type III abdominal radical hysterectomy (ARH) lymphadenectomy.

Method(s): From 1997 to 2008, we tried type III LRH for cervical cancer in 337 patients. Of these, 330 procedures were successful. These patients were matched 1:1 for age age, size of tumor, parametrial involvement, lymph node metastasis, and neoadjuvant chemotherapy to 862 patients who underwent type III ARH during the same study period. The surgical and survival outcomes were compared between the two groups.

<u>Result(s)</u>: A total of 282 patients in LRH group were successfully matched to 282 patients selected from the ARH group. There were no differences in age, FIGO stage, histologic type, tumor size, stromal invasion more than 2/3, parametrial involvement, resection margin involvement, lymphovascular space invasion, lymph node metastasis, adjuvant therapy, mean operating time, the number of lymph nodes retrieved, and the frequency of intraoperative and postoperative complications between the two groups. The LRH group had significantly lower transfusion requirement, less blood loss, faster return of bowel movement, shorter time interval to adjuvant therapy, shorter postoperative hospital stay and higher number of lymph nodes retrieved. After mean follow up time of 43 months (range, 3–139 months), There was no difference in DFS and OS between the two surgery groups. Also dividing patients in two groups according to tumor size (<2 cm or>2 cm), no difference has been found in DFS and OS between the two surgery groups.

<u>Conclusion(s)</u>: LRH with lymphadenectomy showed similar efficacy and safety to ARH with lymphadenectomy in the treatment of patients with FIGO stage IA2–IIA cervical cancer. However, the surgical outcomes were more favorable in LRH group. Therefore, LRH with lymphadenectomy is the preferred method of surgical management for this malignancy.

Laparoscopic Extraperitoneal Para-aortic Lymph Node Dissection in Gynecologic Cancers

Kung Liahng Wang, MD, JR Chen, MD, MC Huang, MD, TC Chen, MD, CL Chang, MD, TH Su, MD, YC Yang, MD

Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan

<u>Purpose of the study</u>:

Cervical cancer is a major gynecological malignancy to be clinically staged. The large discrepancy between clinical and surgical staging remains to be a foremost concern. Most unfortunate predicaments are associated with the under diagnosis of lymph node metastasis. The proper identification of node-positive patients allows individualized therapy and provides prognostic information.

Surgical staging is associated with morbidity, regardless of methodologies, including laparotomy with or without extraperitoneal approach. Laparoscopy can provide a pathologic sample of radiologically negative nodes and is associated with lower morbidity in comparison to a large incision. Additionally, an extraperitoneal approach to the paraaortic node dissection has been associated with less radiation-associated gastrointestinal morbidity.

The laparoscopic extraperitoneal pelvic lymphadenectomy in patients with early cervical cancer was introduced by Dargent in 1987 and the technique was further extended for the extraperitoneal dissection of the common iliac and aortic nodes in 2000. This novel technique has been commented to gain acceptance by Querleu et al in 2003. To investigate the feasibility and safety of laparoscpic extraperitoneal approach of the paraaortic node dissection on patients with gynecologic cancer.

Method(s):

- Our surgical procedure is described below.
- 1. intraperitoneal laparoscopy to look for intraperitoneal disease
- 2. initiation of left extraperitoneal approach
- 3. finger dissection to create extraperitoneal space
- 4. insertion of accessory trocars
- 5. development of pneumo-extraperitoneal space
- 6. identification of left ureter and iliac vessels to create space to aortic area
- 7. identification of right ureter and right common iliac artery
- 8. identification of inferior mesenteric artery and inferior vena cava
- 9. performance of lymph node dissection
- 10. removal of lymph nodes by tissue bag and sent for frozen section
- 11. marsupialization of the extraperitoneal space for drainage

Result(s):

From 2006–2009, we performed 40 cases of laparoscopic extraperitoneal surgical staging. We had no major post–operative complications.

Conclusion(s):

We concluded that laparoscopic extraperitoneal surgical staging is safe and feasible.

Abdominal radical trachelectomy for invasive cervical cancer patients who desire preserving fertility

Hiroaki Kobayashi, MD, PhD, K. Okugawa, MD, PhD, H. Yahata, MD, PhD, S. Ogawa, MD, PhD, K. Sonoda, MD, PhD, T. Kaku, MD, PhD, N. Wake, MD, PhD

Dept. of Gynecology and Obstetrics, Graduate School of Medical Scineces, Kyushu University, Fukuoka, Japan

Purpose of the study: To preserve fertility of invasive cervical cancer patients, we started abdominal radical trachelectomy (ART) from June 2005 after approval of IRB. The validity of eligibility criteria and operation procedures is discussed.

<u>Methods</u>: Our eligibility criteria for ART are mainly: (1)squamous cell carcinoma (FIGO Ia2 to early IIa) and adenocarcinoma (Ib1) not over 3cm and 2cm in width, respectively; (2)MRI indicating at least 1cm free space between the tumor edge and the amputation site of cervix. After sufficient explanation as to the experimental nature of ART and the various troubles in future pregnancy, the informed consent was obtained from each case. Surgical procedures of ART are based on the nerve–sparing abdominal radical hysterectomy (ARH), except for preservation of uterine arteries, prophylactic cerclage around the residual cervix and the anastomosis between uterine body and vaginal canal. Only in the cases without lymph node metastasis confirmed by intraoperative pathological examination, cervix is removed together with the sufficient parametrium and vaginal wall. ART procedure is converted to ARH if we fail to keep 5mm tumor free margin in the amputated cervix.

<u>Results</u>: Within 38 patients fulfilling the preoperative criteria, 35 cases underwent ART and 3 cases, showing positive lymph nodes confirmed by intraoperative examinations, were received RAH. Within 35 cases, 3 patients received adjuvant chemotherapy due to relatively deep stromal invasion and/or vessel permeation. One patient lost her fertility after postoperative pelvic irradiation due to finding micrometastasis in lymph node by a postoperative histological re-examination. Main surgical complications were postsurgical infection occurred near the vaginal anastomosis site, but all cases were easily cured by antibiotics. Another complication was cervical stenosis, and some cases required the cervical dilatation under anesthesia. During 23 months of a mean follow-up period(1–52 months), none of the cases recurred and a patient delivered a child in 28 weeks' gestation.

<u>Conclusions</u>: ART seems to be safely performed by almost equivalent skill to a conventional ARH. Although long follow-up and accumulation of cases are essential, our present eligibility criteria are considered proper.

Evolving Radiotherapy in Cervical Cancer; from 2D to 4D-IGRT

Chomporn Sitathanee, MD

Radiation Oncology Division, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Radiotherapy (RT) has been an important part of cervical cancer treatment. Its roles include radical treatment in patients who are not surgical candidates, adjuvant treatment after surgery, salvage treatment for recurrent disease, and palliative treatment in metastatic disease. The two main modalities of RT are external RT using photon beam and brachytherapy. Both techniques have evolved substantially during the past decade, from standard 2-dimensional field design and dose calculation based on bony structures or fixed reference points to 3-dimensional computer-based conformal RT/ brachytherapy. Despite significant improvements in the primary treatments for cervical cancer, including concurrent chemoradiotherapy, 20-40% of the patients still develop recurrent disease at local and/or distant sites. Management of pelvic recurrence is complicated. Treatment options depend on many factors including disease extent, previous treatment (esp. RT), and patient condition. Unfortunately, not many patients are candidates for surgery. Exenteration can be done in highly selected situations, such as centrally-located lesions, but with the cost of operative morbidity and mortality. Patients with side-wall and inoperable central lesions have more limitations on options for further management. Historically, salvage surgery and/or conventional RT yields a 5-year survival of less than 15%. Delivery of a therapeutic dose of radiation to the abdomen and pelvis is limited by the sensitivity of surrounding normal tissues including small bowel, stomach, kidneys, liver, spinal cord, bladder, rectum, and even bony structures. Novel RT technologies such as intensity modulated RT (IMRT), image-guided RT (IGRT), and stereotactic RT have allowed higher radiation doses to be delivered to the tumors. CyberKnife (Accuray Inc., Sunnyvale, CA), a frameless image-guided robotic radiosurgery system, is a new technology for whole body stereotactic RT. This involves multiple non-isocentric convergent beams combined with targeting accuracy using real time tumor tracking. It allows delivery of high ablative doses of radiation to the tumor while sparing nearby normal tissues due to rapid dose fall-off. Noninvasive frameless nature of the CyberKnife makes multiple treatments (fractionation) of the whole body feasible. This topic will review technique, clinical use, and early results of the CyberKnife stereotactic body radiosurgery in cervical cancer.

Are we justified for concomitant chemo-radiation in Advanced Stage Cancer Cervix?

Shyam Kishore Shrivastava¹, Mahantshetty U¹, Tongaonkar HB², Gupta S³, Engineer R¹, Kerkar RA³, Maheshwari A³, Dinshaw KA¹

Department of Radiation Oncology, Tata Memorial Hospital, Parel, Mumbai, India¹, Department of Gynae Oncology, Tata Memorial Hospital, Parel, Mumbai, India², Department of Medical Oncology, Tata Memorial Hospital, Parel, Mumbai, India³

Background and Rationale: The main stay of treatment has traditionally been radical radiation therapy and over decades the survival rates have achieved a plateau of 30 – 45% at 5 years. Over the last decade there have been studies on the use of chemo-radiotherapy in carcinoma cervix. Over 19 randomized trials have been published addressing the issue of chemo-radiotherapy. However, heterogeneous data, poor randomization, inadequate number of patients, sub-optimal radiotherapy, non-uniform use of chemotherapeutic drugs, its sequencing and poor documentation have not yet provided the evidence to substantially alter the practice. The Cochrane and Canadian meta-analyses have to a large extent tried to address the role of concomitant chemo-radiation, but Carcinoma Cervix Stage III accounted for only 30–35% and moreover evaluation with optimal radiation schedules and comparison of late toxicities still remains unanswered. What is more important is that the cisplatin is relatively inexpensive and is available worldwide. This means that cisplatin-based chemo-radiation is affordable in the developing countries where carcinoma cervix still forms the major cancer. However, the role of chemo-radiation in Carcinoma Cervix Stage IIIB in a developing countries including India still remains unexplored. With an aim to evaluate the role and benefit of chemo-radiation in-patients with cervical cancer we proposed this randomized study.

Patient and Methods: Patients with histologically proven cervical cancer (Squamous Carcinoma only) FIGO IIIB after obtaining written inform consent are randomize to either the Standard arm of Radical Radiation Therapy alone or the study arm of Concurrent Chemo-radiation with Cisplatin (40 mg/m2 weekly x 5#). With an expected improvement in absolute survival by 10% for stages IIIB, α -error of 0.05, power of detection of 80% and 10% patients more to compensate for lost-to-follow-up and major violations, a total of 850 patients will be randomized with stratification for stages and brachytherapy treatment.

Results: In this ongoing randomized study, 627 patients were randomized till November 2008. Currently, we present an audit of 528 patients randomized till December 2007. Of 528 patients, 14 are on treatment and 514 have completed treatment. The treatment related grade III toxicities in the form of Gastrointestinal (3% Vs 4%), genitourinary (2% Vs 3.5%), anemia (1% Vs 6.8%), neutropenia (1% Vs 5.2%) and thrombocytopenia (1% Vs 3.5%) were higher in chemoradiation arm and required active support more often than radical radiation arm. With a median follow-up of 24 months till 2007, 48 patients in radiation alone while 37 patients in Chemoradiation arm had recurrences. The patterns of recurrences were comparable in both the arms.

Conclusions: Concomitant Chemoradiation although feasible appears to be associated with higher incidence of Grade III hematological and gastrointestinal toxicities. These toxicities need active support for completion of planned treatment. In this ongoing randomized study, completion of accrual, comparison of toxicities (acute and late) and outcome is essential to evaluate the exact role of concurrent chemoradiation in advance cervical cancers. An interim analysis is ongoing to assess the toxicities and early outcome.

An audit of Phase II Randomized Trial Comparing Intensity Modulated radiation Therapy (IMRT) with Conventional Radiation Therapy in Stage IIB Carcinoma Cervix

Shyam Kishore Shrivastava, Mahantshetty UM, Jamema SV, Kinhikar RK, R Engineer, DD Deshpande, Tongaonkar HB, KA Dinshaw

Tata Memorial Hospital, Parel, Mumbai, India

Introduction: Carcinoma Cervix is the commonest malignancy in Indian women and leading cause of cancer mortality in India. Radiotherapy [external beam radiotherapy (EBRT) and Intracavitary Brachytherapy (ICBT)] forms the mainstay of treatment for cancer of the cervix. In recent past, concurrent chemoradiotherapy schedules have shown an increase in loco regional control rates and overall survival but at the cost of increase in hematological and GI toxicities. The emerging newer precision radiation techniques especially IMRT, have shown potential for better critical structures sparing and dose escalation to the target. Our pilot study showed a 15 - 22% reduction in high dose regions to rectum, bladder and small bowel region. To evaluate these potentials systematically, we undertook a phase II randomized in carcinoma cervix with an intention to reduce acute grade III radiation enteritis and grade II / III bladder and rectal late sequelae to less than 5% and accrual of 200 patients.

Materials and Methods: After obtaining from eligible patients, inform consent were randomized to Conventional EBRT [40 Gy /20#/4 weeks (midline block in antero-posterior portals) or IMRT arm [50 Gy/25 #/5 weeks]. All these patients received 5 weekly insertions of High Dose Rate ICBT (7 Gy to point A)] and 5# of concurrent weekly cisplatin (40 mg/m²).

Results: In this ongoing study, and till September 113 patients has been randomized. For first interim analysis done in December 2008, 86 patients were randomized and completed treatment. The compliance rates were comparable in both the arms. Acute Grade II (26 patients in both arm) and Grade III Gastrointestinal was seen in 9 (conventional arm) Vs 6 patients in IMRT arm. Similarly, Grade II/III neutropenia was seen in 8 patients in conventional Vs 5 patients in IMRT arm. The response rates were similar in both the arms. With a median follow up 17 months(Mean: 18; 3–45 months) 6 patients in conventional arm (local: 1; pelvic nodal: 1; loco-regional: 2; para-aortic: 1; loco-regional+distant: 1) while 3 patients (local: 1; loco-regional: 1; distant only: 1) in IMRT arm had recurrences so far. Three patients in IMRT while 1 patient in conventional arm had grade II while 3 and 1 patient had Grade III radiation proctitis. All these patients improved symptomatically with steroid enema and argon plasma coagulation. Two patients in IMRT have had grade III radiation cystitis which improved with either fulguration or hyperbaric oxygen therapy.

Conclusion: In this Ongoing Phase III Randomized Trial in Carcinoma Cervix FIGO IIB, the audit so far suggests that moderate dose escalation with IMRT is tolerated well. The acute gastrointestinal and hematological radiation toxicities are fewer with IMRT. The comparison of late radiation sequelae and locoregional control rates needs completion of accrual and further follow-up. Integration of IGRT with the current study would aid in precise treatment delivery and more meaningful interpretation of the toxicity and outcome data.

New Trends of Treatment for Cervical Cancer: The Singapore Experience: the use of the GOG score to tailor postop management for early stage cervical cancer

Chia Yin Nin, Namuduri Ramapadmavathi Devi, Yam Kwai Lam Philip, Lim Yong Kuei

Department of Gynaecologic Oncology, KK Women's and Children's Hospital, Singapore

Introduction

At present, there is no standardized adjuvant management of high risk nodes negative early cervical cancer (FIGOI–IIa) post radical hysterectomy. Delgado et al from the Gynaecology Oncology Group (GOG) first derived a prognostic risk scoring system (called the GOG score) using clinical tumor size, LVSI and depth of tumor invasion to guide the use of adjuvant radiation. Since 1997, KK Women's and Children's Hospital Gynaecology Oncology Centre has adopted the GOG scoring system to help tailor postoperative adjuvant radiation in nodes negative early stage cervical cancer post radical hysterectomy.

Purpose of Study

To evaluate the outcome of the use of the GOG score to tailor post operative adjuvant radiotherapy in node negative high risk early stage cervical cancer after radical hysterectomy.

Method

Retrospective review of case notes of all patients who had underwent radical hysterectomy for FIGO stage 1b to 2A cervical cancer in KK Women's and Children's Hospital, Singapore from January 1997 to December 2007, was carried out.

The protocol for adjuvant radiation is a followed:adjuvant radiation not indicated for GOG score<40, small field pelvic radiation was administered to those with GOG score 40 to 120 and for those with GOG score>120, standard field pelvic radiation was given. GOG Score is calculated by multiplying the relative risk for the depth of tumour invasion into stroma x tumour size x capillary space involvement. Data collected include epidemological data, relapse data, survival data and radiation related morbidity.

Results

There were 191 patients who underwent primary radical hysterectomy during the study period. 110 patients were in stage 1b1, 11 patients were in Ib2 and14 patients were in stage IIa. One hundred and ninety one patients were negative for nodal involvement, parametrium invasion and resection margins. The GOG score was applied to this group to tailor adjuvant radiation of which 62 patients were had a GOG score of less than 40, 44 had a GOG score of 40 to 120 and 27 had a GOG score of>120. Adjuvant radiation was given to 65 patients according to protocol.

At a median follow-up of 74 months, 132 patients are alive and free of disease. Pelvic recurrence was noted in one patient. Despite salvage chemotherapy, she passed away due to disease progression. Two other patient passed away from old age and inter current illness, not related to cancer. Morbidity is acceptable with mainly grade 1 and 2 toxicity.

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Conclusions

Kridelka et al reported a prospective preliminary result (n=25) that showed significant benefit in the DFI among high risk patients categorized by GOG score treated with adjuvant small field radiation for GOG score>120. In comparison, we are more aggressive in our treatment protocol, treating patients with GOG score>40 and our study demonstrated excellent survival outcome with acceptable morbidity using this approach to treatment.

We hence recommend the use of GOG score routinely to guide adjuvant therapy in this group of patients.
P-01 Follow-up Date of patients with patients with LSIL

Eunseop Song, Jeehyun Park, Wooyoung Lee Inha University Hospital, Incheon, Korea

Purpose of the study: To analyze clinical data of patients with LSIL

<u>Method(s)</u>: From October 1996 to February 2009, clinical records of patients with LSIL were reviewed, retrospectively. Every cytologic smear was done by SurePath[™][TriPath Imaging Inc, Burlington,NC, USA]. HPV tests were done by Hybrid capture-II (HC-II) assay (Digene, Newton, MA, USA) or Mygene[™] (Seoul, Korea). Every biopsy was done under the guide of colposcopy.

<u>Result(s)</u>: During more than 12 years, there were 152 patients with LSIL. The distribution of age is 21 to 75 years old (41.1 \pm 11.2). 77 patients underwent follow-up at least more than 1 month (14.6 \pm 15.4, 1 \sim 79), and 75 patients did. When LSILs were found first, 75 patients got HPV test and there were 51 (68.0%) positive and 24 (32.0%) negative patients. 77 patients did not. When LSILs were found first, 84 underwent punch biopsies of the cervix. There were 30 (35.7%) patients with cervicitis, 2 (2.4%) with HPV infection, 44 (52.4%) with CIN 1 and 8 (9.5%) with CIN 2. 68 patients did not get biopsies. Only 18 (11.8%) underwent follow-up biopsies, and there was 1 patient (5.6%) who had CIN 2 after 24 months of LSIL. She did not get biopsy at first. Among the patients who underwent follow-up by cytology, only one patient (1.3%) contracted HSIL 27 months later.

Conclusion(s): There were 68% positivity of HPV and 9.5% of CIN 2 among patients with LSIL. During follow-up, 5.6% of patients contracted CIN 2.

P-02 Nestin Expression in Cervical Intraepithelial Neoplasia and Cervical Cancer

Jae Yun Song, MD, PhD¹, Jae Kwan Lee, MD, PhD¹, Nak Woo Lee, MD, PhD¹, Bom Woo Yeom, MD, PhD², Kyu Wan Lee, MD, PhD¹

Department of Obstetrics and Gynecology, Korea University College of Medicine, Seoul, Korea¹, Department of Pathology, Korea University College of Medicine, Seoul, Korea²

Purpose of the study: Nestin is an intermediate filament protein expressed in proliferating cells during embryonic development of the central nervous system (CNS) and considered to be a neuronal stem cell/progenitor cell marker. Nestin has been detected in various cancers and reported to have a correlation with differentiation, invasion, and metastasis. This study investigated the expression of nestin in normal cervix, CIS, and invasive cervical cancer.

<u>Method(s)</u>: The expression of nestin was immunohistochemically analyzed from 49 normal cervix, 41 CIS, and 39 invasive cervical cancer tissues by the use of a paraffin-embedded tissue array. Immunostaining was evaluated by intensity, proportion of stained cells, and pattern of expression.

<u>Result(s)</u>: The expression of nestin was positive in 63.4% (26/41) for CIS and 43.6% (17/39) for invasive cervical cancer, but only 26.5% (13/49) for normal tissues (P=0.002). Strong positive staining/large proportion staining were 15.4% (6/39) / 61.5% (24/39), 53.7% (22/41)/36.6% (15/41) in the invasive cervical cancer and CIS tissues, respectively (P<0.001)/(P=0.043). The diffuse stain with basal layer was positive in 94.9% (37/39) for invasive cervical cancer and 90.2% (37/41) for CIS, but only 24.5% (12/49) of the samples were positive in normal tissues (P<0.001).

<u>Conclusion(s)</u>: Nestin can be used as a useful marker for the diagnosis of cervical cancer and may be an indicator of cervical cancer initiation.

P-03 A predictor for treatment failure after loop electrosurgical procedure of CIN to CIS of the uterine cervix

Chan Yong Park, MD, KB Lee, MD, JW Shin, MD

Department of Obstetrics & Gynecology, Gachon University of Medicine & Science, Inchon, Korea

Purpose of the study: To investigate the risk factors of persistent disease after loop electrosurgical procedure (LEEP) of cervical intraepithelial neoplasia (CIN) II to carcinoma in situ (CIS).

<u>Method(s)</u>: Using a prospectively maintained CIN database at our department, we reviewed a total of 321 patients who had undergone LEEP for the treatment of biopsy-confirmed CIN II to CIS between March 2006 and February 2008. We defined treatment failure as residual disease after repeat treatment. Post-conization follow-up was performed every 3 months during the first year and then each 6 months during the next year.

<u>**Result(s)**</u>: The risk factor of treatment failure was positive surgical margin (p=0.009). The risk factors of positive surgical margin were high grade intraepithelial lesion (HSIL) in preoperative Pap smear (p=0.00), high risk HPV subtypes in preoperative HPV subtyping (p=0.00), \geq CIN III in final diagnosis (p=0.002). Based on multivariate analyses, HSIL in preoperative Pap smear (p=0.00) and CIN III in final diagnosis (p=0.01) were identified as significant risk factors for positive surgical margin.

<u>Conclusion(s)</u>: Positive surgical margin was the risk factor of treatment failure.

P-04 Risk factors of recurrence for high grade cervical intraepithelial neoplasia after carboxydioxide vaporization

Kouichiro Kawano, MD, PhD, S. Nishio, MD, PhD, K. Fujiyoshi, MD, PhD, K. Ushijima, MD, PhD, T. Kamura, MD, PhD Kurume University, Kurume, Japan

Purpose of the study: We perform carboxydioxide (CO₂) laser vaporization for the case of high grade cerical intraepithelial neoplasia (HG–CIN) whose entire lesion was recognized by colposcopy and which has no suspicious findings of microinvasive cancer preoperatively. However, we sometimes encounter recurrence of HG–CIN after vaporization. The objective of this study was to reveal risk factors of recurrence of HG–CIN.

<u>Method(s)</u>: One hundred seventy nine in 217 patients who received vaporization due to HG–CIN between January 2001 and December 2006 in Kurume University Hospital with a follow–up period after surgery of at least 12 months were enrolled in this study. All patients were screened for recurrence by Pap test and colposcopy after surgery. Recurrence was defined as a patient who had HG–CIN confirmed by biopsy at any time in this study. Clinical and pathological parameters for all patients with HG CIN were obtained for analysis. Fischer's exact test was used for univariable analysis. After excluding the insignificant factors, multivariable logistic regression analysis was used to identify the independent predictive factor for recurrence.

<u>Result(s)</u>: Median age of patients was 32 (17–5) years old. Histological diagnosis was CIN2 in 17 pts, and CIN3 in 162 pts, respectively. Recurrence was identified in 36 pts (20.1%). Median time to recurrence after surgery was 6 (1–47) months. Twenty nine pts (80.5%) were recurred within 12 months after surgery. Both of univariate and multivariate analysis revealed that endocervical disease and multiquadrant (3 or 4 quadrant) disease. Furthermore, risk of recurrence was higher in 4 quadrant disease than 3 quadrant disease.

<u>Conclusion(s)</u>: Benefit of vaporization was minimally invasive and no increase of preterm delivery. We identified that endocervical disease or multiquadrant disease was high risk for recurrence. Therefore, indication of vaporization might be reconsidered in the case of no desire for fertility with these risk factors.

P-05 Human Papillomavirus (HPV) L1 Capsid Protein and HPV Type 16 as Prognostic Markers in Cervical Intraepithelial Neoplasia 1

Young Sam Choi, MD.¹, Woo Dae Kang, MD.¹, Seok Mo Kim, MD.¹, Yoo Duk Choi, MD.², Jong Hee Nam, MD.², Chang Soo Park, MD.², Ho Sun Choi, MD.¹

Department of Obstetrics and Gynecology, Chonnam National University Medical School, Gwangju, Korea¹, Department of Pathology, Chonnam National University Medical School, Gwangju, Korea²

Purpose: The aim of the study was to determine whether human papillomavirus (HPV) L1 capsid protein and the HPV genotype can predict the disease course as prognostic markers for cervical intraepithelial neoplasia 1 (CIN1).

<u>Method(s)</u>: Immunohistochemical staining was performed for HPV L1 capsid protein in 101 women who had been confirmed to have CIN1 by histology and HPV high-risk infection by HPV genotyping. The disease course was analyzed by follow-up histology according to the HPV L1 capsid protein and HPV genotype over a minimum of 12

months.

<u>Result(s)</u>: CIN1 regressed spontaneously in 60.4% of the women;most cases of regression occurred within 1 year (90.9% of regression cases). HPV L1 capsid protein–positive patients had a spontaneous regression rate of 72.7% (48/66) and a rate of persistent disease or progression to higher grade disease of 27.3% (18/66). HPV L1 capsid protein–negative women had a regression rate of 37.1% (13/35), and a rate of persistent disease or progression of 62.9% (22/35;p<0.001). HPV16–infected patients had a regression rate of 38.6% (17/44) and a rate of persistent disease or progression of 61.4% (27/44), whereas non–HPV16–infected patients had a regression rate of 77.2% (44/57) and a rate of persistent disease or progression of 22.8% (13/57;p<0.001).

Conclusion(s): HPV L1 protein expression is closely related to spontaneous disease regression, but HPV16 infection is related to persistent disease or progression to high grade lesions in patients with CIN1.

P-06 Intention to Obtain Human Papillomavirus Vaccination among Taiwanese Undergraduate Women

Ya-Min Cheng^{1,2}, Yu-Yung Hsu³, Ken-Fu Hsu¹, Cheng-Yang Chou¹

Department of Obstetrics and Gynecology, College of Medicine, National Cheng Kung University¹, Institute of Clinical Medicine, College of Medicine, National Cheng Kung University², Department of Nursing, College of Medicine, National Cheng Kung University, Tainan, Taiwan³

Purpose of the study: examine health beliefs and intention toward HPV vaccination among undergraduate college women in Taiwan

<u>Method(s)</u>: A convenience sample of 968 undergraduate female students was recruited from universities located in South Taiwan. A self-administered questionnaire requested demographic information, gynecologic history, awareness of HPV and HPV vaccine, health beliefs, and vaccination intention.

<u>Result(s)</u>: Of the 845 female students providing data, half were aware of HPV, and over half were aware of the HPV vaccine. 63% of the students reported a high intention to obtain the HPV vaccination. Demographic factors predicting HPV vaccination included: age, family history of gynecologic cancer, personal history of gynecologic symptoms, sexual experience, and awareness of HPV and the vaccine. Health belief factors predicting HPV vaccination included: personal susceptibility of disease, perception of disease severity, perceived attributes of HPV. Recommendation from others was a facilitator to HPV vaccination. On the other hand, Cost of vaccine and adverse effect of vaccine were barriers to HPV vaccination

Conclusion(s): Improving college women's HPV vaccination rate will require educational campaigns, specifically focused on the efficacy, safety, and benefits of the HPV vaccine and the attributes of HPV infection.

P-07 Cost-effectiveness Analysis of HPV vaccination in Taiwan

Raoh-Fang Pwu, Ph.D.^{1,2}, Chih-Hsien Liao, MPH^{2,3}, Ines Hang-Iao Chow, MPH.¹, San-Lin You, PH.D.^{4,5}, Chao-Hsiun Tang, Ph.D.^{1,6}, Chi-An Chen, MD.⁷, Yen-Huei Tarn, Ph.D.²

School of Health Care Administration, Taipei Medical University, Taipei, Taiwan¹, Center for Drug Evaluation, Taipei, Taiwan², Institute of Health Care Organization Administration, National Taiwan University, Taipei, Taiwan³, Genomics Research Center, Academia Sinica, Taipei, Taiwan⁴, School of Public Health, National Defense Medical Center, Taipei, Taiwan⁵, Gynecology Research Center, Taipei Medical University Hospital, Taiwan⁶, Department of Obstetrics and Gynecology, National Taiwan University Hospital, National Taiwan University, Taipei, Taiwan⁷

<u>Purpose of the study</u>: Cervical cancer is a serious public health problem in developing countries, including Taiwan. To prevent cervical cancer, Taiwan has introduced cancer screening programs for decades. With the implementation of National Health Insurance that provide routine Pap smear, the decline in incidence and mortality rates in cervical cancer are readily observed. However, HPV vaccines have been developed quite rapidly recently and decision makers are facing more complex options regarding cervical cancer prevention strategies.

<u>Method(s)</u>: This study adopted a health payer perspective for the evaluation. The study model was developed with cervical cancer natural history in Taiwanese women. It was further incorporated with epidemiological parameters, vaccine effectiveness, screening tool performances and cost parameters. The model was built to evaluate the different options of adding HPV vaccination program (for women aged 12 and with or without catch-up) to the current Pap smear screening programs. Quality adjusted life years (QALY) and incremental cost-effectiveness ratio (ICER) were estimated for the comparisons between various strategies. One-way sensitivity analysis and probabilistic sensitivity analysis were conducted to explore the robustness of the results.

<u>Result(s)</u>: Results from the base case analysis show that, inclusion of a HPV vaccination program for the cohort aged 12 can be considered as cost-effective (ICER value 1,010,000 NTD/QALY) comparing with annual Pap smear program only. Results of sensitivity analysis suggest that the results are robust. Catch-up programs under evaluation also showed borderline cost-effectiveness. Further analyses on different vaccination assumptions are still needed. <u>Conclusion(s)</u>: Although a constant decrease in cervical cancer incidence and mortality is to be expected after introducing a population-wide HPV vaccination program in Taiwan, the reduction predicted by this model is lower than expected from clinical trials. This is due to several factors, such as low coverage rate and the long time horizon required for generating the maximum benefit of the vaccination in population. In the context of limited resources, for further reducing cervical cancer in Taiwan, HPV vaccination programs need to be weighed against other public health alternatives.

P-08 Human papillomavirus infection and cervical neoplasia in Taiwan: A long-term follow-up cohort-study

Hui-Chi Chen, Ph.D.¹², Chang-Yao Hsieh, MD.³, San-Lin You, Ph.D.¹, Ching-Yu Lin, Ph.D.⁴⁵, Chien-Jen Chen, Sc.D.¹², CBCSP-HPV Study Group

Genomics Research Center, Academia Sinica, Taipei¹, Graduate Institute of Epidemiology, National Taiwan University, Taipei², Department of Obstetrics & Gynecology, National Taiwan University Hospital, Taipei³, School of Medical Laboratory Science and Biotechnology, Taipei Medical University, Taipei⁴, Yuan–Shan Research Institute, King Car Food Industrial Co. Ltd., I–Lan, Taiwan⁵

Purpose of the study: Human papillomavirus (HPV) is the major determinant of cervical neoplasia. We aimed to estimate association between genotype-specific HPV infection and cervical neoplasia in Taiwan.

Method(s): We collected written informed consent, information on sociodemographic characteristics, reproductive and sexual history, and personal and family history of cancer via a structured questionnaire of 11,923 participants. The cervical cells of 10,602 women were collected for HPV DNA genotyping using the HPV blot method. HPV carcinogenicity was classified according to the International Agency for Research on Cancer (IARC) Working Group criteria. Papanicolaou smears were used to diagnose cervical neoplasia and histological confirmed cervical cancer cases were ascertained by data–linkage with National Cancer Registry. **Result(s):** The overall HPV infection prevalence was 24.5%, and 13.0% of IARC Group 1 types. The most common IARC Group 1 types were HPV52 (2.8%), HPV16 (2.3%), HPV18 (2.1%), HPV56 (2.1%), HPV33 (1.5%), HPV58 (1.4%), and HPV39 (1.1%). In 56 prevalent cervical cancer cases, 96.4% of IARC Group 1 types was detected, HPV16 (48.2%) was the most common followed by HPV52, HPV31, HPV33 and HPV18. The age-specific prevalence of high-grade squamous intraepithelial lesion (HSIL) and cervical cancer was highest in participants infected with HPV 16 and HPV 58 with age-adjusted odds ratio (95% confidence intervals) of 53.2 (30.6–92.6) and 33.6 (17.2–65.9), respectively. The incidence of cervical cancer and cytological HSIL+ were 204.8 and 311.5 per 100,000 person-year for cytologically normal women with IARC Group 1 types infection during long-term follow-up, and the age-adjusted hazard ratios were 18.4 (9.7–34.9) and 8.7 (5.1–14.6) in comparison to women without HPV infection at baseline. Of 69 incident cervical cancer cases, 30.4% of them had HPV16/18 infection and 56.5% had HPV16/58/52/33/31/18 infection.

<u>Conclusion(s)</u>: In Taiwan, HPV infection of IARC Group 1 types was the major determinant for cervical neoplasia. HPV16 is the most oncogenic HPV type followed by HPV58. The higher etiological fractions attributable to HPV16/58/52/18 or HPV16/58/52/33/31/18 infection than HPV16/18 infection indicates the prevention of HPV58/52/31/33 in addition to HPV 16/18 would be more beneficial.

P-09 Evaluation of Signal Pattern of High-Risk Human Papillomavirus in Thin-Layer Cervical Specimens Using a Novel Fluorescence In Situ Hybridization Assays

Chih–Ming Ho, M.D., Ph.D.¹³⁴, Bor–Heng Lee, MSc⁵, Shwu–Fen Chang, M.D., Ph.D⁶, Tsai–Yen Chien, M.D¹, Shih–Hung Huang, M.D², Chiu–Cho Yan⁵, Weng–Fang Cheng, M.D., Ph.D⁷⁸

Gynecologic Cancer Center, Department of Obstetrics and Gynecology, Cathay General Hospital, Taipei, Taiwan¹, Department of Pathology, Cathay General Hospital, Taipei, Taiwan², School of Medicine, Fu Jen Catholic University, Hsinchuang, Taipei Hsien, Taiwan³, School of Medicine, Taipei Medical University, Taipei, Taiwan⁴, King Car Food Industrial Co, Ltd, Yuan Shan Research Institute, Elan, Taiwan⁵, Graduate Institute of Medical Sciences, Taipei Medical University, Taipei, Taiwan⁶, Graduate Institute of Clinical Medicine, National Taiwan University, Taipei, Taiwan⁷, Department of Obstetrics and Gynecology, College of Medicine, National Taiwan University, Taipei, Taiwan⁸

Purpose of the study: To evaluate a novel florescence in situ hybridization (FISH) assay for detecting high-risk human papillomavirus (HR-HPV) DNA and signal pattern in liquid-based cervical cytology specimens with different grades of cervical lesions.

<u>Method(s)</u>: A total of 196 liquid-based cytology specimens from patients with squamous intraepithelial lesions (SILs) were analyzed using our novel FISH assay. The results from the assay were compared with HPV E6 type-specific PCR as a golden standard. The signal pattern (punctate, mixed punctate and diffuse, and diffuse) detected by FISH was compared with E6 mRNA and correlated with histologic classification.

<u>Result(s)</u>: Our findings showed that FISH and E6-type specific PCR had fair to good agreements in detecting HPV DNA across all grade of CIN (Kappa coefficient, 0.37 to 0.73). Among 44 samples of FISH negative and E6 type-specific PCR positive in HPV 16, 18, 31, 33, 52, and 58, 82% (36/44) of E6 mRNA were not detected, in contrast to 41% (48/118) of FISH positive and E6 type-specific PCR positive in HPV 16, 18, 31, 33, 52, and 58 (p<0.0001). In addition, among HR-HPV DNA positive cases tested by FISH assay, the specificity of predicting CIN3 using punctuate pattern is higher than that using E6 mRNA (96.3% vs. 44.8%). The punctate pattern was 0% in patients with <CIN 1 lesions, 8.7% for CIN 1 lesions, 6.1% for CIN 2 lesions, 34.0% for CIN 3 lesions (p=0.001), and the odds ratio were 8.7 times (2.7~27.8, p<0.0001) for punctate pattern versus mixed punctate and diffuse pattern, and diffuse pattern to predict CIN 3 lesions.

<u>Conclusion(s)</u>: The novel FISH assay seems comparable to PCR for detecting HPV DNA in liquid-based cervical cytology specimens with CIN lesions. Punctate signal pattern by FISH assay can be more biologically and clinically relevant for detecting CIN3 lesions.

P-10 Immunoglobulin A secretion in saliva induced by AS04-adjuvanted HPV-16/ 18 vaccine

Yong Wook Jung, MD¹, Sang Wun Kim, MD¹, Eun Ji Nam, MD¹, Jae Hoon Kim, MD¹, Jae Wook Kim, MD², Young Tae Kim, MD¹ Department of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Korea¹, Department of Obstetrics and Gynecology, Kwandong University College of Medicine, Goyang, Korea²

Purpose of the study: This study was performed to evaluate IgA secretion in saliva induced by AS04-adjuvanted HPV-16/18 vaccine.

Method(s): Twenty-eight subjects, who showed seronegative on HPV 16/18, were enrolled in this study. To exclude HPV-16/18 oral infection, DNA analysis for HPV 16/18 using PCR was performed in patients'saliva. Twenty-two of them received AS04-adjuvanted HPV-16/18 vaccine and the others were injected with aluminum hydroxide placebo. The vaccine or placebo was administered intramuscularly on a 0, 1, 6 month schedule. Patients'saliva was collected before HPV vaccination and 7 months after vaccination. The level of HPV-16/18 VLP specific IgA in saliva was determined by ELISA.

<u>Result(s)</u>: All subjects who received the vaccine were seroconverted for HPV 16/18. There was no subject who showed seropositivity for HPV 16/18 in placebo group. In addition, the subjects who were injected with placebo had no IgA immune response for HPV 16/18 in saliva. In subjects who received AS04-adjuvanted vaccine, IgA for both HPV 16 and 18 VLP Ag was detected in 68.2% (15/22). The signal intensity was significantly higher in subjects who had HPV 16/18 VLP IgA immune response as compared with placebo or HPV-16/18 VLP IgA negative group (HPV 16, 0.147 vs. 0.029 vs. 0.052, P= 0.027;HPV 18, 0.213 vs. 0.089 vs. 0.073, P=0.014, respectively). There was no difference in IgA level between subjects who had no IgA response after vaccination and placebo group.

<u>Conclusion(s)</u>: This study indicates that AS04 adjuvanted HPV-16/18 vaccination induces IgA secretion in saliva. It might contribute to examining the role of AS04-adjuvanted HPV-16/18 vaccine in preventing not only HPV infection of uterine cervix, but oropharyngeal HPV infection.

P-11 Outcomes of human papillomavirus infection according to the genotypes

Chul-Min Lee, M.D.¹, Eung-Soo Lee, M.D.²

Sanggye Paik Hospital, Inje University, Seoul, Korea¹, Ilsan Paik Hospital, Inje University, Seoul, Korea²

Purpose of the study: To investigate the prevalence of HPV genotypes and following cervical cytopathology.

Method(s): 711 subjects who were referred from community clinics carrying cervical cytology of ASC–US or higher were included in the analysis from Jan 2005 to Dec 2008. High risk HPV DNA types such as 16,18,31,33,35,39,45,51,52,53,54,56,58,59,66, 68 were tested using microarray. CIN II+ and invasive carcinoma was diagnosed pathologically in 24.2% and 7.0%, respectively.

<u>Result(s)</u>: HPV DNA type 33 showed high PPR (71.4%, OR 8.3 [3.2–21.9]) for CIN II+, while type 16 retained PPR of 55.3%. Type 58, 31, 18, 52 are those genotypes with over 40% of PPR (50.0, 46.4, 43.5, 43.3, respectively). Although FNRs of individual genotypes were less than 25% for CIN II+ and less than 8% for invasive carcinoma, The sensitivity of high risk types overall for detecting CIN II+ and invasive carcinoma was 68.4% and 84.0%, respectively. Genotype 16, 58, 33 are more sensitive in prospecting invasive carcinoma (44.0%, 18.0%, 12.0%, respectively) than other high risk types.

Conclusion(s): Attention should be paid when high-risk HPV infection was detected. More careful follow up is warranted in those with specific genotypes of HPV are infected. A nation-wide study is expected to determine the prevalence of HPV genotypes.

P-12 Evaluation and comparison of HPV genotypes in cervical lesions by the microbead-based array and DNA sequencing method

Young Lae Cho, MD¹, Soon Do Cha, MD², Dong Chun Park, MD³, Sung Ha Lee, MD³, Keun Ho Lee, MD³, Young Jae Kim, MD⁴, Sei Jun Han, MD⁵, Woong Shick Ahn, MD³

Kyungpook National University Hospital, Daegu, Korea¹, Keimyung University Dongsan Hospital, Daegu, Korea², The Catholic University of Korea, Seoul, Korea³, Hanyang University, Seoul, Korea⁴, Chosun University Hospital, Gwangju, Korea⁵

Purpose of the study: The Luminex-based HPV genotyping method is a new high-throughput assay capable of simultaneously typing 26 HPVs including 15 high-risk and 11 low-risk genotypes. To evaluate the clinical accuracy of the Luminex-based genotyping of HPV, we performed HPV DNA sequencing and compared the results with that of the Luminex-based HPV genotyping

<u>Method(s)</u>: 848 cervical samples from Korean women were tested for HPV genotyping in this study. Genomic DNA of cervical lesion was used as a template for amplifying HPV L1 consensus region for all HPV types with PGMY09/PGMY11 primers. Then amplified PCR products was labeled with biotin followed by hybridizing with HPV type-specific oligonucleotide probes coupled to fluorescence-labeled polystyrene beads. For the evaluation of the results of the Luminex-based HPV genotyping, purified HPV L1 consensus PCR products were analyzed by DNA sequencing with newly designed HPV type-specific primer targeted in hyper-variable sequence of consensus L1 region. Sequences of HPV types detected by Luminex were verified by the BLAST program.

Result(s): Among 848 samples, 335 samples were detected as HPV-positive including 283 of single HPV genotype (single infection), 33 of double HPV genotypes (double infection), 11 of at least triple HPV genotypes and 8 of other HPV genotypes and 513 samples were detected as HPV negative. To verify Luminex-based HPV genotyping, Genotyped samples, 848 were confirmed by sequencing. In 800 samples (94.3%) of 848 samples, the HPV types of the HPV DNA sequencing test were in agreement with types of the Luminex-based HPV genotyping test. In single infection, Luminex-based HPV genotyping showed high accuracy of 94.3% (267/283). An accuracy of whole match of double and triple infection was 79.5% (35/44) and partial match was 15.9% (7/44). **Conclusion(s):** Luminex-based HPV genotyping system is valuable for detecting HPV subtypes with patients' samples since it has high accuracy for detecting HPV subtype

P-13 Study for early cervical neoplasia confirmed by cervical conization

Hong-Bae Kim, MD, Hyoung-Jun Kwon, MD

College of Medicine, Hallym University, Seoul, Korea

Purpose of the study: To investigate the accuracy rates of cytology, punch biopsy in early cervical neoplasm, including severe dysplasia, carcinoma in situ, microinvasive carcinoma confirmed by conization

<u>Method(s)</u>: During the 5 years from 2005 to 2008 conization was performed on 103 patients and then 62 patients early cervical neoplasia was proven by conization at the Gynecologic oncologic department of the Hallym University Kangnam Sacred Heart Hospital. We performed cytologic test with cytobrush, 4-quardrent punch biopsy, electrosurgical diathermy or LLETZ Retrospectively chart review, The accuracy of cytology, punch biopsy, conization were investigated.

<u>Result(s)</u>: The mean age was 44 years old. Average gravida was about 2.5. The results of cytology were severe dysplasia & carcinoma in situ–66% (20/30), microinvasive cancer–26% (7/26), true invasive cancer–16% (1/6). The accuracy of cytology was 45% and underestimation rate was 51%. The result of punch biopsy were severe dysplasia & CIS=86% (26/30), microinvasive cancer–46% (12/26), invasive cancer–16% (1/6). The accuracy of punch biopsy was 63% and underestimation rate was 37%. The final result were that severe dysplasia–8 cases, CIS–22 cases, microinvasive cancer–26 cases, true invasive cancer–6 cases. We observed complications of conisation that bleeding 5 cases (4.8%), infection 4 cases (3.9%), cervical stenosis 2 cases (1.9%)

<u>Conclusion(s)</u>: These results suggest that a composite diagnosis with cytology, punch biopsy is necessary for a correct evaluation. These results confirm the risk of over-looking invasive disease by conventional preconisation evaluation. Management for early cervical neoplasia, we recommend conisation as the best conservative procedure, and diagnostic method in preservation of reproductive function and management of patients with early cervical neoplasia of the cervix.

P-14 Conservative management for stage Ia1 squamous cell carcinomas of the uterine cervix with positive resection margin after conization

Woo Young Kim, Suk–Joon Chang, Ki–Hong Chang, Seung–Chul Yoo, Hee–Sug Ryu Ajou University School of Medicine, Suwon, Korea

Purpose of the study: To evaluate the efficacy of cold knife conization with electrocauterization followed by conservative management in patients with stage Ia1 uterine cervical carcinoma.

<u>Method(s)</u>: Medical and histopathological records were reviewed retrospectively. One hundred eight patients with stage Ial uterine cervical carcinoma were treated by cold knife conization with electrocauterization only or followed by hysterectomy. Disease recurrence was defined as a histologic diagnosis of cervical intraepithelial neoplasia (CIN) II or higher grade lesions. **Result(s)**: Forty patients underwent conization followed by hysterectomy and 14 (35%) out of these had residual lesion at cervix. The rest sixty eight patients underwent conization only without further surgical intervention. Forty patients had clear resection margin without recurrence. Twenty eight patients had involved resection margin. (Exocervix (+) :11 cases, Endocervix (+) :17 cases) There were seven cases of recurrence; one case in Exocervix (+), six cases in Endocervix (+) **Conclusion(s)**: Cold knife conization with electrocauterization appears to be safe treatment option for patients with stage Ial cervical squamous cell carcinoma, if careful follow-up is guaranteed in patients having CIN III at exocervical resection margins. However, patients having CIN III or higher lesion at endocervial resection margin should be managed surgically. (reconization or hysterectomy)

Keywords: microinvasive carcinoma, cold knife conization, electrocauterizaion, resection margin, conservative management

P-15 Feasibility of conservative management for stage IB1 cervical cancer with invasion depth of less than 5mm (microinvasive carcinoma)

Mi-Kyung Kim¹, Hee Seung Kim¹, Hyeong Soo Lim¹, Taek Sang Lee², Jae Weon Kim¹, Noh-Hyun Park¹, Yong-Sang Song¹, Soon-Beom Kang¹

Department of Obstetrics and Gynecology, Seoul National University, College of Medicine, Seoul, Korea¹, Department of Obstetrics and Gynecology, Seoul National University, College of Medicine, Borame Hospital, Seoul, Korea²

Purpose of the study: The aim of this study was to evaluate the rate of parametrial involvement in FIGO stage IB1 cervical cancer patients with depth of invasion of 5mm or less, and to evaluate the feasibility of more conservative surgery in this subset of patients. **Method(s):** A retrospective analysis was performed in 275 patients with stage IB1 cervical cancer who underwent primary surgical treatments at Seoul National University Hospital from 2003 to 2008. Of these, patients with depth of invasion of 5mm or less were the subjects of this study. Patients who received neoadjuvant chemotherapy were excluded. Pathologic reports were reviewed to collect the data on depth of invasion, tumor size, and presence of lymphovascular space involvement (LVSI), parametrial invasion, and lymph node metastasis.

Result(s): During the study period, 89 cases with invasion depth of less than 5mm were assessed. Mean depth of invasion was $3.09\pm$ 1.36mm, and mean diameter of width was 21.1 ± 11.4 mm (range, 7–55mm). Lymphovascular space involvement was found in 9 patients (10.1%), and was related to the width of tumor (*P*=.037). Lymph node metastasis was found in 4 patients (4.5%), including two (3.8%) of 52 patients with invasion up to 3mm and two (5.4%) of 37 patients with invasion of 3.1–5mm (*P*=.939). However, none of the patients had metastasis to the parametrial tissue.

With a median follow-up period of 27 months (range, 1–71 months), one recurrence (1.1%) was observed. It was a local recurrence which was resolved by chemoradiation.

<u>Conclusion(s)</u>: These results indicate that more conservative surgical treatment omitting radical parametrectomy can be administered for microinvasive stage IB1 cervical cancer. However, pelvic lymphadenectomy is still required.

P-16 Laparoscopic radical trachelectomy in young women with early cervical cancer

Joo-Hyun Nam, Jeong-Yeol Park, Won Duk Joo, Hang Jo You, Dae-Yeon Kim, Jong-Hyeok Kim, Yong-Man Kim, Young-Tak Kim

Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea

Purpose of the study: We report preliminary results of our work using laparoscopic radical trachelectomy (LRT) in young patients with early cervical cancer who desire to preserve fertility, with respect to surgical, oncological, and obstetrical outcomes.

<u>Method(s)</u>: Twenty five patients (under age of 40 years) with early stage cervical cancer, who wished to preserve their fertility tried LRT at Asan Medical Center, Seoul, Korea, from Oct 2004 to Feb 2008. Demographic, clinicopathologic, surgical, and follow-up data were obtained from the medical records of patients. All patients agreed to telephone interviews to assess their obstetrical outcomes.

<u>Result(s)</u>: In four patients, the planned LRT procedures were abandoned because intraoperative frozen section examinations revealed a parametrial extension of the tumor in one patient and pelvic lymph node involvement in three patients. Of 21 patients who succeeded in LRT, Twenty patients had stage IB1 disease and one patient had stage IIA disease. Histologic type of tumor was squamous cell carcinoma in 16 patients, adenocarcinoma in 3 patients, and adenosquamous cell carcinoma in 2 patients. The mean tumor size was 1.56cm (range, 0.4–3.5cm). The mean age was 29 years (range, 22–36 years). Mean body mass index was 20.7kg/m2 (range, 17.5–24.6kg/m2). Fourteen patients were nulliparous. Mean operating time was 303 min (range, 120–520 min) and mean estimated blood loss was 326mL (range, 50–1000mL). Five patients required perioperative transfusion. There were no severe perioperative complications required further treatment or reoperation. The mean postoperative hospital stay was 9 days (range, 4–18 days). Postoperative adjuvant chemotherapy was given to on a patient who had stage IIA tumor larger than 3cm. After a mean follow-up time of 24 months (range, 5–48 months), there was one recurrence and death of disease. Regular menstruation returned in 21 patients 3 months after surgery. Five patients attempted to conceive and two succeeded.

<u>Conclusion(s)</u>: LRT may be a safe and useful alternative to LRH for women with early cervical cancer who want to preserve their fertility. To confirm this suggestion, a large prospective study is needed.

P-17 Fertility Preservation by Photodynamic Therapy in Early Cervical cancer or Endometrial Cancer

Chan Lee, Sang Geun Jung, Sun Young Lee, Yoon Young Hwang, Seung Jo Kim

Comprehensive Gynecology Cancer Center, Bundang CHA General Hospital, college of Medicine, CHA University, Seongnam, Gyeonggi-do, Korea

<u>Purpose of the study</u>: To evaluate the response and efficacy of PDT in patients with cervical or endometrial cancer who want to preserve fertility.

<u>Method(s)</u>: A study of 23 young women with early cervical or endometrial cancer, who received PDT with or without chemotherapy for fertility sparing from May 2002 to March 2008, was performed.

<u>Result(s)</u>: The mean age was 29 years old. Histology of cervical cancer included squamous cell carcinoma (n=8), glassy cell cancer (n=3). All histology of endometrial cancer were endometrioid adenocarcinoma. 10 of 11 patients with cervical cancer were in stage I and one patient was stage IIA. We performed lymph node dissection to the patients who had evidence of enlarged LN on imaging study or had large tumor size (>2cm). In endometrial cancer, clinical stages of 12 patients were evaluated initially by imaging studies (CT, MRI or PET). There were 1 patient with deep myometrial invasion and 6 patients with superficial invasion and another 3 patients were confined to endometrium. The remaining 2 patients were recurrent status. The mean follow-up duration was 37 months. Of 11 patients in cervical cancer, 11 patients (100%) were cured with PDT. In endometrial cancer patients, all patients were cured with PDT, but 3 patients were recurrent 2 recurrent patients were treated with additional PDT and are alive without disease now. Remaining one patient wanted operation. 7 patients were delivered of fullterm-babies.

<u>Conclusion(s)</u>: The photodynamic therapy could be a promising tool in the management of cervical and endometrial cancer to preserve fertility.

P-18 Characteristics and prognosis of cervical cancer in young women

Hei-Yu Lau, MD¹, JY Tseng, MD¹, SY Chiu, MD¹, CM Juang, MD^{1,2}, YJ Chen, MD¹, NF Twu, MD¹, MS Yen, MD¹, KC Chao, MD¹ Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, National Yang-Ming University, Taipei, Taiwan¹, Institute of Public Health, National Yang-Ming University, Taipei, Taiwan²

<u>Purpose of the study</u>: To compare the characteristics and prognosis of cervical cancer in young women (under 30 years) with those of older women (over 30 years)

<u>Method(s)</u>: A retrospective analysis was conducted. Eligible patients diagnosed with FIGO stage IA–IIA cervical cancer who underwent surgical procedures between January 1983 and December 2007 at the index hospital were enrolled in our study. Demographic, clinical, and histological parameters of patients under 30 years and over 30 years were compared.

<u>Result(s)</u>: Of the 2443 eligible patients, 30 (1.2%) were 30 years or younger. There was no significant difference between those \leq 30 and >30 years with respect to body mass index, smoking habits and staging distribution. The proportion of non-squamous cell carcinoma was higher in patients 30 years or younger compared with in patients over 30 years (14/30, 46.7% vs 299/2413, 12.4%; P<0.001). A higher rate of parametrial involvement was found in the younger group of patients compared with those over 30 years (10/30, 33.3% vs 289/2413, 12.0%; P=0.001). Patients under 30 years had a higher rate of distant metastases compared with older patients (60% vs 49.7%; P=0.036).

<u>Conclusion(s)</u>: Non-squamous histology, parametrial involvement, a higher rate of distant metastases, and poorer prognosis are more common in women aged 30 or younger with cervical cancer than in older women with the disease. Due to the aggressive characteristics of cervical cancer in young women, optimal adjuvant therapy with closer follow-up is mandatory for this specific group of patients.

P-19 laparoscopic surgical staging for locally advanced cervical carcinoma: comparison with primary concurrent chemoradiation

Dae Gy Hong, M.D.¹, Gun Oh Chong, M.D.¹, Soon Do Cha, M.D.,PhD.², Young Lae Cho, M.D.,PhD.¹, Il Soo Park, M.D.,PhD.¹, Yoon Soo Lee, M.D.,PhD.¹

Department of Obstetrics and Gynecology, Kyungpook National University Graduate School of Medicine, Daegu, Korea¹, Department of Obstetrics and Gynecology, Keimyung University School of Medicine, Daegu, Korea²

Purpose of the study: This study was designed to report our clinical results of laparoscopic surgical staging comparing with primary concurrent chemoradiation in locally advanced cervical cancer.

<u>Method(s)</u>: We performed 20 cases of laparoscopic surgical staging and 69 cases of primary concurrent chemoradiation for locally advanced cervical cancer from January 2000 to January 2006. We retrospectively analyzed the pathologic reports and clinical data and compared two groups. The Kaplan–Meier and log–rank test were used.

Result(s): There was 8 cases of operation related complication in laparoscopic surgical staiging. The mean follow up period is 59 months for staging group, 71months for primary concurrent chemoradiation group. The 5–year survival rate of each group is 68% in staging group and 62% in chemoradiation group. There is no statistically significance (P=0.79). The 5–year disease free survival rate of each group is 52% in staging group and 55% in chemoradiation group. There is no statistically significance (P=0.28).

<u>Conclusion(s)</u>: The benefits of laparoscopic surgical staging for locally advanced cervical cancer are not clear. In this study the laparoscopic surgical staging with postoperative adjuvant therapy has not benefits on survival outcome compared with primary concurrent chemoradiation.

P-20 Urological evaluation after nerve sparing radical hysterectomy

Chung Won Lee, Keun Ho Lee, Sung Eun Namkoong

Department of Obstetrics and Gynecology, Seoul St. Mary hospital, Seoul, Korea

Purpose of the study: Nerve sparing radical hysterectomy (NSRH) was introduced to prevent urological complications in cervical cancer patients. We are aim to compare urodynamic changes after NSRH.

<u>Method(s)</u>: From Jan 2000 through Dec 2003, cervical cancer stage Ia2 to IIB patients who underwent type III radical hysterectomy were reviewed. Urological evaluations such as postoperative complications, timing of removal of indwelling catheter were evaluated. Urodynamic study was done before and after surgery.

<u>Result(s)</u>: One hundred thirty nine patients were performed by TRH and 22 patients were performed by NSRH. There were no differences between age, stage, treatment of neoadjuvant chemotherapy and type of adjuvant chemotherapy. And also size of tumor, operation time, resection margin of vagina, depth of tumor invasion, resected lymph node, perivasucular or lymphatic metastasis were not differed.

The First day to try removal of indwelling Foley catheter was 11.2th and 9.0th day in TRH and NSRH, respectively. The day to remove Foley catheter successfully was 15.2th, and 10.3th day, respectively (p<0.05). Residual bladder volume were also differed in both groups (173.1ml in TRH, 152.6ml in NSRH). Urodynamic study revealed there were no effect detrusor noninhibitory contraction, maximal cystometric capacity, maximal urethral closing pressure, and stress urinary incontinence.

Conclusion(s): There were favorable outcomes on postoperative urodynamic changes in NSRH compared to TRH.

P-21 Analysis of risk factors for parametrial involvement and the need for parametrial resection in early stage cervical cancer

Jeong-Yeol Park, Jong-Hyeok Kim, Dae-Yeon Kim, Yong-Man Kim, Young-Tak Kim, Joo-Hyun Nam

Department of Obstetrics and Gynecology, College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Korea

Purpose of the study: The aim of this study was to analyze the risk factors for parametrial involvement in patients with early stage cervical cancer who underwent radical hysterectomy and to discriminate the patients who have low risk for parametrial involvement. **Method(s):** We searched patients with FIGO stage IA1–IIA cervical cancer who underwent radical hysterectomy at Asan Medical Center, Seoul, Korea, between 1990 and 2007 using cancer registry and computerized database of the institution. Patients who underwent preoperative chemotherapy, radiation therapy, or concurrent chemoradiation therapy were excluded.

<u>Result(s)</u>: During the study period, a total of 1178 patients met the inclusion criteria. Parametrial involvement was histologically proven in 102 patients (8.7%). Lymphovascular space invasion (Odds radio [OR]=8.05, 95% confidence interaval [CI]=5.11–12.67, P=< 0.001), tumor size larger than 2cm (OR=3.59, 95% CI=2.33–5.32, P<0.001), deep stromal invasion more than 2/3 (OR=5.08, 95% CI=2.76–9.36, P<0.001), vaginal involvement (OR=4.41, 95% CI=2.82–6.88, P<0.001), advanced stage (OR=3.57, 95% CI=2.14–5.94, P=<0.001), and lymph node metastasis (OR=6.19, 95% CI=3.68–9.63, P<0.001) were significantly associated with parametrial involvement. The incidence of lymph node metastasis in patients with and without parametrial involvement was 49% and 13%, respectively. Parametrial involvement had significant risk factor for lymph node metastasis (OR=6.192, 95% CI=3.98–9.63, P<0.001). Patients with parametrial involvement had significantly poor disease free survival and overall survival (P<0.001 and <0.001, respectively). In patients with negative lymphovascular space invasion, negative lymph node metastasis, stromal invasion less than 2/3, tumor size less than 2cm, the incidence of parametrial involvement was 0.9% (2/224).

<u>Conclusion(s)</u>: Lymphovascular space invasion, tumor size larger than 2cm, deep stromal invasion more than 2/3, vaginal involvement, advanced stage, and lymph node metastasis were significant risk factors for parametrial involvement. The role of parametrectomy needs to be reevaluated in patients without these risk factors.

P-22 Influence of post operative adjuvant concurrent chemo radiation on survival for high-risk early stage cervical cancer—KK hospital experience

Rama P Namuduri, Yin Nin Chia, Kwai Lam Yam, YK Lim

Department of Gynecological Oncology, KK Women's and Children's Hospital, Singapore

Purpose of the study: The study was conducted to evaluate the efficacy of post operative concurrent chemoradiation [CCRT] and its influence in survival in stage 1B to II A cervical cancer patients who underwent radical hysterectomy and pelvic lymphadenectomy.

<u>Method(s)</u>: From January 1997 to October2007 we reviewed retrospectively medical records of 340 patients who had undergone radical hysterectomy and pelvic lymphadenectomy at KK Women's and Children's hospital for early cancers IB to II A. Fifty six patients with high risk factors such as positive pelvic lymph nodes, parametrial involvement, or positive resection margins recruited in the study. CCRT was recommended for them. Adjuvant chemotherapy consisted of cisplatin (70mg/m2on day 1) and 5fluorouracil (5FU;1000mg/m2on days 2–5) for 4 cycles every 4 weeks beginning 2–3weeks after surgery. Pelvic radiotherapy was started concurrently at the 2nd and 3rd cycle of chemotherapy. We analyzed disease free survival, overall survival and pattern of recurrence and side effects of CCRT.

<u>Result(s)</u>: Three forty patients underwent radical hysterectomy and pelvic lymphadenectomy in the study period. 56 patients with high risk features identified. 48 patients received CCRT. Follow up period ranges from 11 to 113 months with a mean follow up period of 48 months.

11patients died of recurrence of disease. The 5 years disease free survival rate was 84.4% and the 10 years disease free survival rate was 63.4%.

Conclusion(s): This study supports good 5 years survival rate with side effects of chemotherapy and radiation treatment in acceptable range.

P-23 The Role of Celecoxib in Cox-2-PGE2 pathways activity, proliferation, apoptosis and tumor size reduction on concurrent chemotherapy and radiation therapy for cervical cancer

Supriadi Gandamihardja, MD¹, Firman F Wirakusumah, MD¹, Herri S Sastramihardja, MD¹, M Nurhalim Shahib, MD¹, M Farid Aziz, MD²

University of Padjadjaran, Bandung, Indonesia¹, University of Indonesia, Jakarta, Indonesia²

Purpose of study: Concurrent chemotherapy and radiation therapy (CT-RT) for late stage cervical cancer has been proved as an effective treatment, but its treatment failure is still high and needs further improvements. Selective COX-2 inhibitor, Celecoxib, has a significant role for increasing apoptosis, reducing proliferation and tumor growth of cancer. Four hundreds miligrams Celecoxib b.i.d administration concomitant with CTRT showed a high incidence of side effect,

The research was purposed to investigate the role of 200mg Celecoxib b.i.d in COX-2-PGE₂ pathway, proliferation, apoptosis, tumor size reduction and correlation between these variables.

Method: A prospective study with pretest–posttest control group design was done in 2008 at the Hasan Sadikin Hospital Bandung by recruiting 20 cervical cancer patients who received Celecoxib and CT–RT, and another 21 patients treated by CT–RT only as control group. Cervical tissues obtained by biopsy were sent for mRNA COX-2 assessment by RT–PCR and COX-2 enzyme, Ki–67, and Caspase–3 as proliferation and apoptosis markers, assessed by immunohistochemistry. Cervical tumor size was measured by transabdominal ultrasonography. All variables were obtained before and after external CT–RT. Data were analyzed by using Wilcoxon test and Pearson's correlation test. **Result:** The results showed a significant effects of selective COX–2 inhibitor to synchronized decrease of mRNA COX–2 and COX–2 enzyme expression level (p<0.01), which represented COX–2-PGE₂ pathways inhibition, reduce Ki–67 expression level (p<0.01), increase Caspase–3 expression level (p<0.01) and tumor size reduction (p<0.01). Another result was significant correlations between COX–2 enzyme expression level and mRNA COX–2, Ki–67 and Caspase–3 expression level ratio and tumor size reduction. **Conclusion:** Celecoxib plays a significant role in increasing tumor volume reduction based upon decreasing of COX–2-PGE₂ pathways activity, which reduces proliferation marked by Ki–67 and increases apoptosis marked by Caspase–3.

Keywords: Late stage cervical cancer, Celecoxib, mRNA-COX-2, COX-2 enzyme, Ki-67, Caspase-3, tumor size reduction

P-24 Cisplatin and etoposide as neoadjuvant chemotherapy in patients with stages IIB-IIIB cervical cancer: A Phase II study

Yoon Young Hwang, MD, Sang Geun Jung, MD, Sun Young Lee, MD, Chan Lee, MD, Seung Jo Kim Comprehensive Gynecologic Cancer Center, Bundang CHA General Hospital, Graduate School of Medicine, CHA University, Kyunngi-do, Korea

Purpose of the study: to evaluate the effectiveness of cisplatin and etoposide as neoadjuvant chemotherapy in patients with advanced stage (stage IIB-IIIB) cervix cancer patients

<u>Method(s)</u>: Between June, 2000 and August, 2004, 73 patients with advanced staged cervix cancer who were treated in Comprehensive Gynecologic Cancer Center, Bundang CHA General Hospital, CHA University were enrolled. These patients had neoadjuvant chemotherapy using cisplatin and etoposide followed by radical hysterectomy with pelvic and paraaortic lymph node dissection. According to pathologic results of surgical specimen, they were treated adjuvant therapy, concurrent chemoradiation or adjuvant chemotherapy. We analyzed the response of neoadjuvant chemotherapy and overall survival of these patients. Also the prognostic factors in cervix cancer were evaluated.

Result(s): In total 73 patients, fifty-five had stage IIB, 2 had stage IIIA, and 16 had stage IIIB. The median age was 55 years (range 34–70), and most patients had squamous cell carcinomas (86%). A total of 280 courses of chemotherapy were administered. Objective responses of neoadjuvant chemotherapy occurred in 67 patients (92%); of these, 8 (11%) were complete and 59 (81%) were partial. Six patients (8%) showed no response to chemotherapy. The overall resectability rate was 89% (65/73). The analysis of the surgical specimens showed complete pathological response in 7 of 65 patients (11%). Microscopic residual disease was found in 8 (12%) and macroscopic pathologic response was found in 50 of 65 patients (77%). 48 patients (73.8%) received adjuvant chemoradiation. For a median follow up of 43 months (range, 5–80), the 5–year survival rate (5YSR) was 82% and 3–year disease–free survival rate (3YDFS) was 76%. In analysis of prognostic factors, stage, parametrial involvement, positive surgical margin and lymph node metastasis were statistically significant (p<0.05).

<u>Conclusion(s)</u>: Cisplatin and etoposide regimen as neoadjuvant chemotherapy in advanced cervix cancer was effective and leaded to improvement of overall survival. But further study such as randomized phase III is need.

P-25 Neoadjuvant chemotherapy in locally advanced uterine cervix cancer

Murat Kairbayev, MD, E. Kukubassov, MD, R. Shalbayeva, MD, A. Touresheva, MD, K. Smagulova, MD

Kazakh Research Institute of Oncology & Radiology, Almaty, Kazakhstan

Purpose of the study: to evaluate results of neoadjuvant chemotherapy in locally advanced uterine cervix cancer.

<u>Method(s)</u>: current study is based on data achieved from 27 patients with FIGO stage IIb–IIIb squamos cell uterine cervix cancer. The median age of patients was 45.33±1.57 years (min 32, max 61).

All patients underwent 2 cycles of NACT:cisplatin 75mg/m² at the 1st day and gemcitabine 800–1000mg/m² at day 1, 8, with repeat after 21 day. After completion of 2 cycles of NACT all patients were evaluated for possible surgery RH with LND. Patients without parametrial involvement after NACT considered eligible for surgery. all other patients were treated by radiation therapy. Treatment effectiveness was evaluated according to clinical examination, ultrasound and MRI. Survival indexes were calculated using Kaplan-Meier method (SPSS for Windows, 15.0).

<u>Result(s)</u>: OR rate was 81.5%. CR rate observed in 2 (7.4%) cases and PR was found in 20 (74.1%) cases. tumor regression allow us to perform radical surgery in 62.9% of primary inoperable cases. In this group 3 patients needed additional postoperative irradiation according to surgical pathological findings.

During observation period 1 patients died from disease at 15 month and 2 patients died at 18 month. Overall survival at 5 years was 75.0±13.0%.

We found that survival indexes were higher in patients where RH with LND was performed compared to those underwent radiation therapy (82.0±3.6% vs. 71.0± 2.7% respectively).

The analyses of survival have been done with respect to some known prognostic factors. Survival in patients with FIGO stage IIb disease was 77.8 \pm 3.9%, and 66.7 \pm 2.7 in FIGO stage IIIb cases. Bilateral parametrial involvement affected worse results compared to unilateral parametrial invasion (62.5 \pm 17.1% vs. 83.3 \pm 15.2%, p<0.05). Regional lymph node metastasis was also negative prognostic factor, because survival in these patients was significantly lower than in patients with negative lymph nodes (66.7 \pm 27.2% vs. 88.5 \pm 16.1%).

<u>Conclusion(s)</u>: NACT in locally advanced cervical cancer shown it's effectiveness with high incidence of OR, and allow to perform radical surgery in 62.9% cases. It was determined that survival in operated patients is 11% higher than in irradiated patients. FIGO stage, parametrial involvement and direct results of NACT are shown to be significant prognostic factors.

P-26 Secular trends of cervical cancer mortality and incidence in Taiwan: Before and after implementation of national screening program

Yun-Yuan Chen, Ph.D.¹, San-Lin You, Ph.D.², Chi-An Chen, MD.³, Lin-Yi Shih, MPH⁴, Shin-Lan Koong, Ph.D.⁴,

Kun-Yu Chao, Ph.D.⁴, Mei-Ling Hsiao, MPH⁴, Chang-Yao Hsieh, MD.³, Chien-Jen Chen, Sc.D¹²,

Taiwan Cervical Cancer Screening Task Force

Graduate Institute of Epidemiology, College of Public Health, National Taiwan University, Taipei, Taiwan¹, Genomics Research Center, Academia Sinica, Taipei, Taiwan², Department of Obstetrics and Gynecology, National Taiwan University Hospital, National Taiwan University, Taipei, Taiwan³, Bureau of Health Promotion, Department of Health, Executive Yuan, Taipei, Taiwan⁴

Purpose of the study: This study aimed to examine secular changes of cervical cancer incidence and mortality of women aged 30 or more years before and after the nation-wide cervical cancer screening program initiated in mid-1995 in Taiwan.

<u>Method(s)</u>: The age-specific numbers of incident cases and deaths during 1991–2007 were obtained from National Cancer Registry and National Death Certification profiles, while population numbers were obtained from National Household Registry profiles. Screening participation rate was derived from National Cervical Cancer Screening Registry database. Age-standardized incidence and mortality were calculated using the world population in 2000 as the standard. The rate ratios for age groups and calendar years were estimated using Poisson regression.

Result(s): The annual screening rate was less than 10% before 1995, and the triennial rate increased from 33.9% to 51.0% during 1997–2007. There was no significant change in age-standardized mortality during 1991–1994, and a significant reduction was observed during 1995–2007 (21.9 to 11.4 in 100,000). The age-standardized invasive cancer incidence decreased slightly during 1991–1994, but strikingly during 1995–2006 (50.2 to 26.2 in 100,000). The age-standardized carcinoma *in-situ* incidence increased slightly during 1991–1994 and significantly during 1995–2000 (23.9 to 65.2 in 100,000), and then decreased 19.6% during 2000–2006. The age-standardized incidence decreased significantly for squamous cell carcinoma after 1995, and slightly for adenocarcinoma after 2001. There were significant increases in mortality and incidence of cervical cancer with age. No significant increase with age was observed for carcinoma *in-situ* incidence.

<u>Conclusion(s)</u>: The national screening program since 1995 has significantly decreased invasive cervical cancer risk in Taiwan.

P-27 Chemosensitivity of Uterine Cervical Cancer Demonstrated by the Histoculture Drug Response Assay

Yong-Man Kim, Shin Wha Lee, Dae-Yeon Kim, Jong-Hyeok Kim, Joo-Hyun Nam, Young-Tak Kim Department of Obstetrics and Gynecology, University of Ulsan, Asan Medical Center, Seoul, Korea

Purpose of the study: Recently chemotherapy in uterine cervical cancer is being emphasized. However, chemotherapeutic strategies are based on only a few clinical trials to find effective drugs. The purpose of this study is to investigate the chemosensitive and chemoresistant indices of uterine cervical cancer using the histoculture drug response assay (HDRA). **Method(s):** Sixty-five fresh tumor tissues were obtained from patients with cervical cancer at the Asan Medical Center, Seoul, Korea between January 2004 and March 2009. Most patients were FIGO stage I and IIA (93.8%) and squamous cell carcinoma (72.3%). The inhibition rates of ten chemotherapeutic agents against these cancer tissues were tested using the HDRA method according to established methods.

<u>Result(s)</u>: Five drugs, carboplatin, cisplatin, paclitaxel, belotecan and topotecan were evaluated as effective agents with inhibition rates greater than 30% in the HDRA; carboplatin 41.0%, cisplatin 35.0%, paclitaxel 33.8%, belotecan 41.4% and topotecan 49.2%. Especially, carboplatin combined with paclitaxel had a 54.0% inhibition rate, which was higher than any other single agent. There were no differences in chemosensitivity according to histopathologic types and FIGO stage. The clinical outcome had a tendency following the data by the HDRA, however, it has been impossible to confirm the correlation between *in vitro* chemosensitivity and clinical outcomes because of the limited data.

<u>Conclusion(s)</u>: The HDRA is a useful *in vitro* chemosensitivity test to decide which drug is effective to each patient. Further studies are necessary to validate the clinical benefit of the HDRA and to advance the individualized chemotherapy in patients with uterine cervical cancer.

P-28 Cervical Cancer Prevention in Developing Country See and Treat Model (Jakarta-Indonesian Perspective)

Laila Nuranna¹, Sigit Purbadi¹, Gatot Purwoto¹, M Farid Aziz¹, Santoso Cornain², Setyawati Budiningsih³, Budiningsih Siregar² Department of Obstetrics and Gynecology, Faculty of Medicine, University of Indonesia Jakarta, Indonesia¹, Department of Pathologic Anatomy, Faculty of Medicine, University of Indonesia Jakarta, Indonesia², Department of Community Medicine Faculty of Medicine, University of Indonesia Jakarta, Indonesia³

Objective: to report the application of the cervical cancer prevention by See and Treat Model which appropriate for country with low resource setting. To know the prevalence of cervical precancerous lesion, and treatment by cryotherapy.

Methods: Research design is an interventional study in community setting for cervical cancer prevention. This study was conducted at 2004 till 2006 in Jakarta. **Results:** Screening programme based on Pap test was difficult to be applied in low resource setting, the alternative methods is Visual Inspection with Acetic Acid (VIA).We should anticipate high number cases of loss of follow up for further treatment, and the alternative is cryotherapy in one single visit or we call SEE and TREAT.

We combined the See and Treat and how to implement at the community in comprehensive approach, which consists of five pillars foundation of 1). Area preparation to have local government support,2). Training, 3). Promotion, 4). See and treat by VIA and cryotherapy, and 5). Referral system.

Report from Jakarta area in 2004 to 2006 on 8.004 respondents, it was study with See and Treat Program with special name of *Proactive–VO (Proactive, Coordinative with VIA, and Cryotherapy)*. Community counseling was performed by PKK (*Pendidikan Kesejahteraan Keluarga*=Family Welfare Empowerment) health cadres.

From 8.004 respondents, it was found 102 (1,28%) precancerous cancer and 5 cases (0,06%) of invasive cervical cancer. From all of the respondents, 24 cases still needed to refer to referral hospital.

Conclusions: VIA is a good alternative screening method, and cryotherapy is a promising way to treat pracancerous lesions in this low resource setting. This *Proactive-VO* model is recommended for cervical cancer prevention.

Key words: Cervical cancer, cancer screening, VIA, cryotherapy, see and treat, screening coverage, cervical cancer prevention model.

P-29 Evidence-Based Performance Measures of Cervical Cancer Care Quality in Taiwan

Mei-Shu Lai, MD.¹, Shin-Lan Koong, Ph.D.², Chun-Ju Chiang, Ph.D.³, Chi-An Chen, MD.⁴, Taiwan Cancer Registry Task Force Institute of Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan¹, Bureau of Health Promotion, Department of Health, Executive Yuan, Taiwan², Genomics Research Center, Academia Sinica, Taipei, Taiwan³, Department of Obstetrics and Gynecology, National Taiwan University Hospital, National Taiwan University, Taipei, Taiwan⁴

Purpose of the study: The purpose of the study was to develop organization-based core performance measures (CPMs) for cervical cancer patients treated in hospitals that participated in cancer quality improvement programmers in Taiwan. **Method(s):** We developed organizationbased CPMs for cervical cancer in three stages: preparation stage, consensus building stage and two stages stakeholder feedback. Three criteria and seven subcriteria were applied in the development process. Indicators listed in a Delphi questionnaire were based on a literature search, indicators developed by relevant institutions and discussion by authors. Each indicator needed to meet inclusion criteria as a final indicator. Evidence-based guidelines, expert opinions from panel group, 27 hospitals and empirical data were all applied to develop and revise the core measures. **Result(s):** As a result of all of these efforts, 25 indicators were selected and revised as organization-based core measures for cervical cancer in Taiwan. There were 10 pre-treatment indicators for screening and diagnosis, 8 treatment-related indicators, and 7 monitoring-related indicators. The CPMs for cervical cancer can be developed systematically and be applied for internal quality improvement and external surveillance.

Conclusion(s): Our experience can be extended to link with pay for performance or certification program in cancer care.

P-30 The uterine cervix cancer in Kazakhstan: scope of the problem

Murat Kairbayev, MD, A. Shibanova, MD, E. Kukubassov, MD, R. Shalbayeva, MD, Zh. Chingissova, MD Kazakh Research Institute of Oncology & Radiology, Almaty, Kazakhstan

Objectives: uterine cervix cancer is the second most common cancer in Kazakhstan. For the last decade the morbidity indexes staying stable at the rate of 7.1 for 100.000 of population in 2001 and 8.0 for 100.000 in 2008. The mortality from cervical cancer tends to slow decreasing from 4.6 in 2001 to 3.8 in 2008. The highest morbidity indexes are among women at age 35 to 60 years. Nearly about 30% of patients diagnosed at advanced stage of disease. Overall 5-year survival rate among cervical cancer patients in Kazakhstan is 60.7%. Totally to the end of 2007 we have 9.269 women alive more than 5 years after treatment.

Purpose of the study: improving cervical cancer care in Kazakhstan

Method(s): In order to improve cervical cancer care in Kazakhstan we started package plan in 2007 which includes three main activities:information, education and prevention. Result(s): Information strategy includes cooperation with mass media:publications in newspapers, publishing bulletins and others. The main goal of such activity was to provide

population with some basic knowledge about cervical cancer and to prepare people for other activities.

Next step consist in reviewing of national standards of cervical cancer treatment because they where not reviewed for more than 10 years. We lay the corner stone for evidence based treatment protocols and divide them into two levels according to local abilities of healthcare in different regions of Kazakhstan. During this activity we organized three educational courses for gynecologic oncologists. These courses include treatment guidelines of gynecological malignancies and surgery of invasive cervical cancer.

The last and main step was the start of first National screening program for cervical cancer in 2008. Whereas availability of cytological laboratories all over the country and enough amount of gynecologists we choose conventional cytological screening. The target population is women between 35 and 60 years old, screening interval now is 5 years. In order to start with Pap smears we organized three seminars for cytologists and 15 workshops for gynecologists in each region of Kazakhstan during 2008. This work is still going on and regional workshops became routine because they helps to keep in touch with gynecologists and control the screening program.

At the end of the first year we diagnosed cytological abnormalities: ASC-21849 (4.76%), LSIL-10695 (2.33%), HSIL-2799 (0.61%), invasive cancer-180 (0.03%).

<u>Conclusion(s)</u>: We still have lot problems with implementing of cytological screening. First of all, Pap-testing and TBS was not common in Kazakhstan, so it's very difficult to achieve good quality of smears and interpretation. The second problem is large territory with sparsely populated areas. But we stay optimistic and going to improve this program in order to decrease morbidity and mortality from cervical cancer.

P-31 Risk of Cytologic Atypical Glandular Cells of Undetermined Significance in Gynecologic Malignancies

Wen-Fang Cheng, M.D., Ph.D.¹², Yu-Li Chen, M.D.⁴, San-Lin You, Ph.D.³, Chien-Jen Chen, Sc.D.³, Yi-Chu Chen, M.S.P.H.³, Chang-Yao Hsieh, M.D., M.S.P.H.¹, Chi-An Chen, M.D.¹

Department of Obstetrics and Gynecology, College of Public Health, National Taiwan University¹, Graduate Institute of Clinical Medicine, College of Medicine, College of Public Health, National Taiwan University², Graduate Institute of Epidemiology, College of Public Health, National Taiwan University⁴, Department of Obstetrics and Gynecology, National Taiwan University⁴

Purpose of the study: To investigate the relationship between screening status, clinical characteristics and risk of gynecologic malignancies, and types of gynecologic malignancies in women with cytologic diagnosis of atypical glandular cells of undetermined significance (AGC-US). **Method(s):** Totally 8,281 women were diagnosed as cytologic AGC-US for the first time in their lives in the nationwide screening population during January 1, 1995 to December 31, 2004. They were divided into screened (5,386 women) and unscreened (2,895 cases) groups according to their screening status. The followed-up histological reports were retrieved for analysis.

<u>Result(s)</u>: There were total 323 women developing gynecologic malignancies during the followed-up period including 271 incident cases of invasive cervical cancer (ICC), 40 incident cases of uterine cancer, and 12 incident cases of ovarian cancer during a mean follow-up of 1.9 years and 50,740 person-years. The previous screening status is a strong risk predictor of developing invasive gynecologic malignancies (HR 1.69 (95% CI 1.20–2.37, p=0.0027)) after adjusting age, educational status, and hospital setting. The biological gradient of gynecologic cancers by age is found in the unscreened group, but it is not noted in the screened group. Compared with general screening population, a significant larger proportion of women with a first time of cytologic AGC–US developed invasive gynecologic malignancies (ICC, p<0.01;uterine cancer, p<0.01;ovarian cancer, p=0.01).

<u>Conclusion(s)</u>: Women with cytologic AGC–US, especially those first diagnosed having AGC–US, those with older age, lower educational status, longer previous Pap smear interval, or even without receiving Pap smear before, were more likely to develop gynecologic malignancies. They should be closely followed, and the physicians should carefully examine the female reproductive tract comprehensively.

P-32 Utility of Serum CA19-9 as a Marker of Recurrence of Endocervical Mucinous Adenocarcinoma with Gastric Phenotype

Atsumi Kojima, M.D.¹, Yoshiki Mikami, M.D.⁴, Noriyoshi Oki, M.D.², Yoshiya Miyahara, M.D.², Tamotsu Sudo, M.D.³, Satoshi Yamaguchi, M.D.², Masaharu Ito, M.D.¹, Ryuichiro Nishimura, M.D.²³

Department of Obstetrics and Gynecology, Ehime University, Ehime, Japan¹, Department of Gynecologic Oncology, Hyogo Cancer Center, Akashi, Japan², Division of Clinical Research, Hyogo Cancer Center, Akashi, Japan³, Department of Diagnostic Pathology, Kyoto University Hospital, Kyoto, Japan⁴

Purpose of the study: Minimal deviation adenocarcinoma (MDA) of the uterine cervix is an aggressive tumor with gastric phenotype, i.e. immunoreactivity for HIK1083 and/or MUC6. We recently reported that a subset of a usual-type endocervical adenocarcinoma also shows a gastric immunophenotype, and proposed the concept of a gastric-type adenocarcinoma (GA) as a distinct entity. GA, which includes MDA, importantly shows an aggressive clinical course. Because patients with GA are at increased risk of recurrence, effective predictive markers are needed for early detection of any recurrence. This study aimed to determine if there was a difference in the patterns of marker elevation between GA and non-gastric type adenocarcinomas (non-GA).

<u>Method(s)</u>: Carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19–9, and CA 125 concentrations were measured in 13 cases, 7 GAs and 6 non–GAs, of stage Ib–IIb endocervical adenocarcinoma that showed recurrence. The sites of recurrence were determined from medical records.

Result(s): There was no significant difference in preoperative serum CA19–9 levels between the two groups (median, mean \pm S.D:73.4, 973 \pm 2289 versus 55.3, 63.9 \pm 61.1U/ml), but at the time of recurrence, GA patients showed significantly higher levels of CA19–9 than non–GA patients (213.5, 181.2 \pm 106.3 versus 18.0, 31.8 \pm 38.8U/ml; *P*<0.05). All GA patients showed CA19–9 values exceeding normal limits. There was no significant difference in either CEA or CA125 levels at any time. Distant metastasis was identified in only one of 7 GA cases (14.3%), but in 5 of 6 non–GA cases (83.3%).

<u>Conclusion(s)</u>: Evaluation of serum CA19–9 level is a useful tool for detecting recurrences of GA, which more frequently occurs at localized sites than as distant metastasis as commonly seen in non–GA cases.

P-33 Cap43/NDRG1/Drg-1 is a molecular target for angiogenesis and a prognostic indicator in cervical adenocarcinoma

Shin Nishio, K. Ushijima, A. Terada, S. Takemoto, N. Fujiyoshi, S. Takemoto, N. Tsuda, K. Kawano, M. Ijichi, F. Murakami, S. Ota, K. Komai, K. Fujiyoshi, T. Kamura

Department of Obstetrics and Gynecology, Kurume University School of Medicine, Kurume, Japan

<u>Purpose of the study</u>: Cap43 is a nickel- and calcium-inducible gene that has been found to play a significant role in metastasis and invasion, as well as in the primary tumor growth of malignant tumors, possibly through its ability to induce differentiation. The majority of studies thus far have suggested a negative correlation between Cap43 expression and cancer progression. However, this plausible role of Cap43 in preventing the cancer progression has been shown to depend on tissue of origin and the tumor type. The aim of this study was to investigate associations between Cap43 expression and angiogenesis and other clinicopathological factor in cervical adenocarcinoma.

<u>Method(s)</u>: The records of 100 women who underwent surgery for International Federation of Gynaecology and Obstetrics (FIGO) clinical stage I–II cervical adenocarcinoma were retrospectively reviewed, and microvessel density (MVD) and expression of both Cap43 and vascular endothelial growth factor (VEGF) were evaluated in the surgical specimens by immunohistochemistry. Significant associations were found between the level of Cap43 expression and the level of VEGF expression, MVD, histologic grade, tumor diameter, stromal invasion, lymphovascular space invasion and lymph node metastasis.

<u>Result(s)</u>: Kaplan–Meier plots demonstrated a clear influence of Cap43 expression on survival time. The median overall survival time of patients whose tumors showed low levels of Cap43 expression was 54.1 months, as opposed to only 36.4 months for patients whose tumors showed high levels of Cap43 expression (log–rank test; *P*=0.0018).

<u>Conclusion(s)</u>: These results suggest that increased expression of Cap43 may be associated with angiogenesis and may a poor prognostic indicator in cervical adenocarcinoma.

P-34 The combination clinicopathological factors, Serum Matrix Metalloproteinase-2 (MMP-2), MMP-9, and Vascular Endothelial Growth Factor (VEGF) as the lymph node metastasis predictor in early stage cervical cancer

Hariadi Yuseran, MD¹, MF Aziz, MD², B Sutrisna, MD²

University of Lambung Mangkurat, Banjarmasin, Indonesia¹, University of Indonesia, Jakarta, Indonesia²

Purpose of the study: Our aim consist of investigating clinicopathological factors and levels of circulating MMP-9, MMP-2 and VEGF in predicting the incidence of lymph node metastasis and then arranged scoring system as well as lymph node metastasis probability prediction.

<u>Method(s)</u>: Case-control study. A series of 82 patients who underwent radical surgery for early stage cervical cancer was used in this study.

<u>Result(s)</u>: In bivariate analysis, the factors had lymph node metastatic risk were age <44 years with OR 4.09 (95% CI: 1.442–11.596, *p*: 0.008). Primary tumor size >40mm with OR 4.45 (95% CI: 1.069–18.551, *p*: 0.040). Stage IIA >4cm with OR 11.33 (95% CI: 1.049–122.387, *p*: 0.046) compare to stage IB \leq 4cm. Poor differentiation with OR 26 (95% CI: 2.936–230.273, *p*: 0.003) and intermediate with OR 10.4 (95% CI: 1.238–87.312 *p*: 0.031). Positive lymphatic and lymphovascular invasion with OR 47.78 (95% CI: 5.956–383.324, *p*: 0.000) and OR 47.78 (95% CI: 5.956–383.324, *p*: 0.000) and OR 47.78 (95% CI: 5.956–383.324, *p*: 0.000) respectively. Serum VEGF level \geq 368.705pg/mL with OR 3.052 (95% CI: 1.075–8.667, *p*: 0.036). Serum MMP–2 level <178.910pg/mL and MMP–9 level \geq 422.031ng/mL with OR 2.951 (95% CI: 0.886–9.826, *p*: 0.078) and OR 2.353 (95% CI: 0.846–6.545, *p*: 0.10) respectively. In multivariate analysis, MMP–9 and VEGF was not statistically significance with *p*: 0.162 and 0.233 respectively, however could be included in scoring calculation.

<u>Conclusion(s)</u>: Age, parity >4, primary lesion size, lymp-vascular invasion, differentiation and high level of VEGF and MMP-9 are the lymph node metastasis risk factors and can be used as the predictor for early stage cervical cancer.

Keywords: cervical cancer, MMP-2, MMP-9, VEGF, lymph node, scoring system

P-35 Effect of VEGF Polymorphisms on Survival in Patients with Early Cervical Cancer

Yun Hwan Kim, Hyun Hoon Chung, Jae Weon Kim, Noh-Hyun Park, Yong-Sang Song, Soon-Beom Kang Department of Obstetrics and Gynecology, Seoul National University, College of Medicine, Seoul, Korea

Purpose of the study: Cervical cancer is an angiogenic tumor which may be related to vascular endothelial growth factor (VEGF) expression. We hypothesized that VEGF genetic polymorphisms may affect survival outcomes in patients with early cervical cancer.

<u>Method(s)</u>: We specifically selected and investigated 4 candidates of genetic polymorphisms within VEGF gene (-2578C>A, -460T>C, +405G>C, and +936C>T) through literature review. The relationship between genetic polymorphisms and clinical outcomes were evaluated among 199 early cervical cancer patients who were treated with surgical resection at Seoul National University Hospital from 2000 to 2004.

<u>Result(s)</u>: Patients with VEGF 405 C/C was associated with the shortness of disease-free survival (adjusted HR=3.18, 95% CI 1.13 to 8.94, P=0.028) and overall survival (adjusted HR=8.86, 95% CI 0.1.40 to 56.08, P=0.020) by Cox proportional hazard model. However, other VEGF polymorphisms have little association with the prognosis of early cervical cancer.

<u>Conclusion(s)</u>: Polymorphisms of VEGF gene may affect survival in patients with early cervical cancer.

P-36 Effect of HIF-1α and VEGF Polymorphisms on Cancer Susceptibility in Early Cervical Cancer

Soon-Beom Kang, MD, Yun Hwan Kim, MD, Hyun Hoon Chung, MD, Jae Weon Kim, MD, Noh-Hyun Park, MD, Yong-Sang Song, MD

Department of Obstetrics and Gynecology, Seoul National University, College of Medicine, Seoul, Korea

Purpose of the study: Cervical cancer is an angiogenic tumor which may be related to Hypoxia inducible factor $1-\alpha$ (HIF-1 α) dependent vascular endothelial growth factor (VEGF) expression. We hypothesized that HIF-1 α and VEGF genetic polymorphisms may affect cancer susceptibility in patients with early cervical cancer.

<u>Method(s)</u>: We specifically investigated 6 genetic polymorphisms within HIF-1 α (1772C>T and 1790G>A) and VEGF gene (-2578C>A, -460T>C, +405G>C, and +936C>T). The association between genetic polymorphisms and cancer susceptibility were evaluated among 215 healthy unrelated subjects and 199 early cervical cancer patients who were treated with surgical resection at Seoul National University Hospital from 2000 to 2004.

<u>Result(s)</u>: The risk of cervical cancer was decreased in subjects with VEGF -2578 A/A genotype compared with C/C or C/A genotypes (adjusted OR=0.39 95% CI 0.16 to 0.96; p=0.040). Although other polymorphisms showed little association with early cervical cancer, increased lymph node metastasis was associated with HIF-1 α 1790 G/A or A/A genotypes, VEGF - 2578 A/A, and VEGF -460 C/C genotype (p=0.024, 0.043 and 0.043, respectively).

Conclusion(s): VEGF genetic polymorphisms could affect cancer susceptibility in patients with early cervical cancer.

P-37 Prognostic significance of Serum Vascular Endothelial Growth Factor-C (Serum VEGF-C) and Lymph-Vascular Space Invasion in Early Stage Cervical Cancer

Heru Priyanto Samadi, MD¹, Andrijono, MD², MF Azis, MD²

Oncology Division – Department of Obstetrics and Gynecology.Faculty of Medicine Sebelas Maret University – Dr. Moewardi Hospital. Solo. Centre Java. Indonesia¹, Oncology Division – Department of Obstetrics and Gynecology.Faculty of Medicine University of Indonesia –Dr. Cipto Mangunkusumo Hospital. Jakarta.Indonesia²

Purpose of the study: The aim of the study was to investigate prognostic value of Serum Vascular Endothelial Growth Factor-C (Serum VEGF-C) and lymph-vascular space invasion as a predictor to lymph node metastasis in early stage cervical cancer.

<u>Method(s)</u>: Fourteen seven consecutive patients with early-stage cervical cancer on January-October 2007 included in this case control study. 14 patient with lymph node metastasis as cases and 33 patient without it as control. 5ml blood examined preoperatively by ELISA method to determined Serum VEGF-C levels.

<u>Result(s)</u>: Cut-off point serum VEGF-C levels in this study was 10.066pg/ml, with 78,57% sensitivity and 96,97% specificity. Lymph node metastasis patient with serum VEGF-C level >10.066pg/ml increase by OR 80, 95% CI 7,99;800,71 and p=0,000. Lymph node metastasis patient with lymph vascular space invasion increase by OR 20, 95% CI 2,32;171,77 and p=0,006. Lymph node metastasis increase by OR 12,5, 95% CI 1,44;108,18 and p=0,022 in patient affected lymph vascular space invasion. Multivariate analysis conclude serum VEGF-C can be use as independent prognostic factor on lymph-node metastasis.

<u>Conclusion(s)</u>: Serum VEGF-C is potential bio-marker as prognostic factor to lymph node metastasis in early stage cervical cancer.

P-38 The accuracy of non-three-layer criteria of endometrial transvaginal ultrasonography in premenopausal women with abnormal bleeding

Masakazu Abe, MD¹, T. Doi, MD¹, Y. Oonishi, MD², T. Noda, MD²

Fujinomiya City Hospital, Fujinomiya, Japan¹, Clinic Ms SOPHIA, Hamamatsu, Japan²

Purpose of the study: Transvaginal ultrasonography for the detection of endometrial disease is very successful for postmenopausal women, but its accuracy in premenopausal women with abnormal uterine bleeding has not been well established. We have previously established the accuracy of our "non-three-layer" criteria of endometrial transvaginal ultrasonography for biopsy recommendation in premenopausal women (Abe et al. 2008). In the current study we have reevaluated the overall diagnostic accuracy of the same criteria by addition of new cases to the previous cases.

<u>Method(s)</u>: Data from 359 consecutive premenopausal patients with abnormal uterine bleeding who underwent transvaginal ultrasonography combined with aspiration endometrial biopsy between 2005 and 2009 was collected. The abnormal findings so called "non-three-layer" criteria were the same (either diffuse or focal hyperechoic texture, regardless of a three-layer; three-layer-like or non-laminar appearance; and linear irregularities). Ultrasonographic findings were recorded and compared with final diagnoses on the basis of histopathologic evaluation. Sensitivity, specificity, positive and negative predictive value, and likelihood ratio were calculated.

Result(s): Histological examination revealed abnormal endometrial histology in 264 patients (73.5%) as 9, 2, 5, 212, 9 and 27 cases of carcinoma, endometrial intraepithelial neoplasia, endometrial hyperplasia, endometrial polyp, endometritis, hormonal abnormality, respectively. The sensitivity and specificity of transvaginal ultrasonography in detecting histological abnormality using non-three-layer criteria was 96.2% and 90.5% with positive and negative predictive value of 96.6% and 89.6%, respectively. Positive and negative likelihood ratio was 10.16 and 0.04, respectively. False positive and negative rate resulted in 9.5% and 3.8%, respectively.

<u>Conclusion(s)</u>: We achieved over 95% sensitivity and over 90% specificity. transvaginal ultrasonography using our diagnostic criteria is an excellent initial diagnostic method with high accuracy for determining whether endometrial biopsy is needed in premenopausal women with abnormal bleeding. Our clinical approach would prevent further invasive diagnostic procedures. We recommend transvaginal ultrasonography using non-three-layer criteria during the proliferative phase combined with endometrial aspiration biopsy when necessary in the workup of premenopausal women with abnormal bleeding as excellent initial diagnostic procedure.

P-39 Outcomes of Radiotherapy for Endometrial Cancer and Its Comarison to Surgical Intervention

Yasuhiko Shiki, MD, M. Chatani, MD, A. Hosoi, MD, M. Isobe, MD, T. Miyake, MD, M. Yamasaki, MD Osaka Rosai Hospital, Sakai, Japan

Purpose of the study: Surgical staging has been accepted as standard therapy in patients with endometrial cancer. In some cases, clinical conditions such as obesity, advanced complications or refusal of surgery make it difficult to perform surgical therapy. We evaluated the effects and complications of radiotherapy for endometrial cancer in these clinical conditions. **Method(s):** 13 cases of endometrial cancer treated with radiotherapy (RT) and 147 cases with surgical intervention at Osaka Rosai Hospital between January 2000 and December 2007 were analyzed retrospectively. Pathological evaluation befor therapy was obtained by endometrial biopsy. High dose rate brachytherapy (combined with external radiation in 5 cases) was the primary therapy in RT group. The degree of myometrial invasion and the presence of metastatic pelvic and para-aortic lymph nodes were inferred using MRI and CT respectively. Kaplan–Meyer survival curve and Log–rank test were used for analysis.

<u>Result(s)</u>: Average age of RT group was older than surgical group significantly (70±12 vs. 58±9 years old) but cases diagnosed as stage 1 were similar in both groups (77% vs. 76%). Median follow-up period of both groups was similar (RT group vs. surgical group: 45 months vs. 53 months). Disease free survival and overall survival at 5 years was significantly better in surgical group (44% vs. 92%, 68% vs. 96% respectively). No severe complications were observed in both groups. **Conclusion(s)**: Survival rates after radiation therapy were inferior to surgical intervention, but radiation therapy for

<u>Conclusion(s)</u>: Survival rates after radiation therapy were inferior to surgical intervention, but radiation therapy for endometrial cancer can be an option for inoperable stage 1 patients.

P-40 Bone Mineral Density in Patients with Endometrial Cancer

Seung-Ho Lee, MD, Chan-Yong Park, MD

Department of Obstetrics and Gynecology, Gachon University Gil Hospital, Incheon, Korea

Purpose of the study: A variety of neoplasms without bone metastasis are related to osteoporosis. Our purpose was to evaluate the bone mineral density (BMD) in patient with endometrial cancer.

<u>Method(s)</u>: We retrospectively analyzed the BMD of spine and femur measured by dual-energy X-ray absorptiometry (DEXA) in 31 patients with endometrial cancer and 61 control women. The control group was treated with surgery for benign disease. All patients with endometrial cancer and the control women experienced menopause. There were no bone metastases in patients with endometrial cancer. We compared age, height, body weight, body mass index (BMI) and BMD of spine and femur between the endometrial cancer and control, and compared BMD between stage I and stage II, III, IV endometrial cancer patients.

<u>Result(s)</u>: There were no differences in the BMD of spine and femur in patients with endometrial cancer and control group. In patients with stage I and stage II, III, IV endometrial cancer, we could not find any differences in the BMD of spine and femur.

Conclusion(s): Endometrial cancer appeared to have no effects on BMD before treatment. But, to define its detailed effect on BMD, prospective study with large sample size is needed.

P-41 Evaluation of prognostic factors and clinical outcomes in uterine sarcoma

Jung-Eun Mok, M.D., Seok-Geun Yoon, M.D., Woo-Chul Kim, M.D., Hong-Jun Choi, M.D., Ho-Suap Hahn, M.D., Yong-Soon Kwon, M.D., In-Ho Lee, M.D., Tae-Jin Kim, M.D., Ki-Heon Lee, M.D., Jae-Uk Shim, M.D., Kyung-Taek Lim, M.D. Department of Obstetrics and Gynecology, Cheil General Hospital and Women's Healthcare Center, Kwandong University College of Medicine, Seoul, Korea

Purpose of the study: To evaluate the impact of several proposed prognostic factors and clinical outcomes in uterine sarcoma as compared the differences between its subtypes.

<u>Method(s)</u>: We analyzed retrospectively medical records of 91 patients diagnosed and treated with uterine sarcoma at the Cheil General Hospital and Women's Healthcare Center from 1988 to 2006.

<u>Result(s)</u>: The mean age of the group was 46.7 (range 20–67). Total 91 patients were enrolled in our study. Thirty-two (35.2%)patients had an endometrial stromal sarcoma (ESS), 28 (30.8%) a leiomyosarcoma (LMS), and 31 (34.0%) a malignant mixed mullerian tumors (MMMT). Univariate analysis demonstrated a statistically significant association between overall survival and histology in favor of patients with ESS (p<0.001). FIGO stage, increased tumor weight (\geq 250g) and high mitotic figure (\geq 10/HPF) were statistically proven to have significant prognostic value on DFS. But no prognostic variables other than FIGO stage demonstrate overall survival gain. Analyzing each of the histological subtypes separately, tumor weight and frequent mitosis are important prognostic indicators for ESS, while stage and tumor grade for LMS and myometrial invasion depth for MMMT. Adjuvant treatment with chemotherapy and/or hormonal treatment had no demonstrable impact on overall survival.

In multivariate analysis, advanced stage remained a significant predictor for overall survival in patients with LMS and MMT, but not in patients with ESS. Furthermore, radiotherapy had a significant impact on overall survival only in patients with MMMT (p<0.002).

<u>Conclusion(s)</u>: In patients with uterine sarcoma, ESS tends to present as frequent extrauterine disease but a favorable outcome in comparison to LMS and MMMT. It seems to be mandatory to differentiate between histologic subtypes in the management of uterine sarcoma.

P-42 Risk of Malignant Indices to Detect Malignant pelvic masses in the preoperative evaluation

Kyung Tai Kim¹, Hong Jue Lee¹, Young Jae Kim¹, Sam Hyun Cho¹, Bo Youl Choi²

Department of Obstetrics and Gynecology, College of Medicine, Hanyang University Seoul, Korea¹, Department of Preventive Medicine, College of Medicine, Hanyang University Seoul, Korea²

Purpose of the study: The preoperative determination of a malignant pelvic mass and referral to gynecologic oncologist has been considered as one of the most important prognostic factors. Several scoring systems have been developed to distinguish between benign and malignant adnexal tumors. RMI (Risk of malignant index) was introduced in 1990 by Jacobs et al for the first time and has been revised three times until 2009 (RMI2, RMI3 and RMI4). We also developed Korean version of RMI (RMIkr) in 2005, however, it has never been validated in Korean population. The aim of this study was to validate the RMIkr and compare it to other RMIs to predict malignancy in an adnexal mass by applying the models to Korean data. **Method(s):** We recruited 327 patients who were diagnosed and received surgical management from 2004 to 2008 in Hanyang university hospital. Exclusion criteria were followings: 1) premenarche, 2) incomplete work-up of preoperative CA125 or ultrasound. We collected the data of age, menopause, a level of CA125, largest tumor size of a mass and ultrasound findings.

Result(s): Of 379 patients, 66 (20.2%) had malignant and borderline disease and 261 (79.8%) had benign pathology. The mean age of the patients with malignant disease was 44.6±2.08 years and 39.2±0.90 years in benign disease. The AUCs of the RMIs ranged from 0.86–0.89. RMI 4 showed highest AUC value (AUC 0.89, 95%CI 0.85–0.94) and the RMIkr showed lowest AUC value (AUC 0.86, 95%CI 0.80–0.92). The RMIkr using Sassone's ultrasound scoring had higher level of sensitivity and lower level of specificity than other RMIs using Jacobs'ultrasound scoring system (84.8%, 65.5% vs. 57.6~62.1%, 94.6~96.6%). RMIkr could detect all the epithelial cancer with stage II–IV, non–epithelial cancer and metastatic cancer. However, the detection rate (%) of Epithelial cancer stage I and borderline tumor were 70% and 60% respectively.

<u>Conclusion(s)</u>: The Korean version of RMI is simple and useful to decide whether optimal cytoreductive surgery is necessary in patients with pelvic mass. However, it has a tendency to refer more benign masses to specialist than other RMIs. It was suggested that ultrasound score was definitive factor for RMIs, therefore, development of new Korean version of RMI including other ultrasound scoring systems could be considered.

P-43 Isoliquiritigenin induces apoptosis in endometrial cancer cells

Chi-Heum Cho, Sang-Hoon Kwon, So-Jin Shin, Soon-Do Cha

Department of Gynecologic Oncology, School of medicine, Keimyung University, Daegu, Korea

Purpose of the study: The objective is to determine the cytotoxicity of isoliquiritigenin (ISL) on endometrial cancer cell and to evaluate its effect on apoptosis in Hec1A endometrial cancer cell lines.

<u>Method(s)</u>: Human endometrial cancer cell lines, Hec1A and Ishikawa, and normal endometrial cell line, T–HESCS, were cultured *in vitro*. The viabilities of three cell lines on ISL were measured. Cell cycle distribution and induction of apoptosis were measured in Hec1A cells after ISL treatment.

<u>Result(s)</u>: ISL significantly reduced cell viabilities of endometrial cancer cell lines but not normal cell line in a dosedependent manner. Cell cycle analysis indicated that ISL treatment increased the proportion of cells in the sub– G_0/G_1 phase. DNA fragmentation and fluorometric TUNEL assays also revealed apoptotic cell death after ISL incubation. ISL treatment markedly up–regulated the expression of cyclin–dependent kinase inhibitor, p21^{Cip1/Waf1} in a p53 independent manner and down regulated the expressions of cyclins and CDKs, with concomitant increase in FAS and cleavage of caspase 7, caspase 8, and caspase 9. In addition, elevation of caspase 3 activity also observed in a dose and time dependent manner.

Conclusion(s): ISL inhibited cell proliferation and triggered apoptosis in human endometrial cancer cell line Hec1A. Hence, ISL can be used as a potentially potent clinical chemotherapeutic agent for treating endometrial cancer.

P-44 The Hyperexpressions of Undifferentiated Markers of Stem Cells in the Endometrium of Patients with Endometriosis

Won-Gyu Kim, M.D¹, Chun June Lee, M.D¹, Jong-Ryeol Choi, M.D², Kyu-Sup Lee, M.D²

Department of Obstetrics and Gynecology, College of Medicine, Gospel Hospital, Kosin University, Busan, Korea¹, Department of Obstetrics and Gynecology, School of Medicine, Pusan National University, Busan, Korea²

Purpose of the study: Recently it was proposed that stem cells may be associated with the pathogenesis of endometriosis. The purpose of this study is to observe whether the endometrial cells of women with or without endometriosis have the morphological characteristics of stem cells in vitro culture, and to investigate for the expressions of undifferentiated markers of stem cells, OCT-4 and CXCR4.

Method(s): A total of 6 women with endometriosis and a total of 10 women without endometriosis or adenomyosis were included in this study. We observed the endometrial cells obtained in the menstrual blood at menstrual cycle day 2 to 4 and cultured, subsequently observed putative very small stem cells separated by ficoll-plaque and cultured. The morphological characteristics of stem cells were observed in vitro culture by microscopy and the expressions of OCT-4 and CXCR4 of endometrial cells were analyzed by real time PCR.

<u>Result(s)</u>: The endometrial cells of patients with endometriosis showed the different morphological characteristics compared with control in vitro culture; heterogenous stromal cells, more common $6-8\mu$ m sized mobile cells less than erythrocyte and more common 20μ m sized hyperchromatic round cells. In vitro culture after the separation of $6-8\mu$ m sized cells by ficoll-plaque, they showed the several characteristics of stem cells; self-renewal, asymmetrical cell division, colony formation and embryoid body-like formation. These cells showed the similar characteristics of very small embryonic-like stem cells; the $6-8\mu$ m sized mobile cells, cell migration or adhesion to supportive cells, sphere formation and nuclear recombination with cell fusion in supportive cells. In the investigation as to the expressions of OCT-4 and CXCR4 by real time PCR, the group with endometriosis were respectively 5.66 times and 17.69 times as high as that without endometriosis (p<0.05).

<u>Conclusion(s)</u>: The expressions of the undifferentiated markers of stem cells, OCT-4 and CXCR4, were significantly higher in the group with endometriosis. This study suggests that stem cells may play a key role in the pathogenesis of endometriosis and OCT-4 and CXCR4, the undifferentiated markers of stem cells, may use a tool for diagnosis or follow-up.

P-45 The Clinicopathologic Characteristics of the Borderline Ovary Tumors

Sang-Young Ryu, M.D., Sang-Il Park, M.D., Kim Kidong, M.D., Beob-Jong Kim, M.D., Moon-Hong Kim, M.D., Seok-Chul Choi, M.D., Eui-Don Lee, M.D., Kyung-Hee Lee, M.D. Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences, Seoul, Korea

Purpose of the study: The aim of this study was to assess the clinicopathologic characteristics of borderline ovary tumors (BOTs).

<u>Method(s)</u>: From 1988 to 2009, 89 patients who were histologically diagnosed with borderline ovary tumors at Korea Cancer Center Hospital were reviewed their medical records. Distribution of clinicopathologic factors such as age, stage, and adjuvant chemotherapy modalities were investigated retrospectively.

<u>Result(s)</u>: The mean age was 40.9 years (range 14–78), and the mean tumor size was 12.7cm (4–25). Histologically, 56 patients (62.9%) were mucinous type, and 61 patients (87.1%) were FIGO stage I disease. 40 patients (54.8%) received fertility-saving operation and 48 patients (78.7%) had no adjuvant therapy after debulking surgery. During the median follow-up of 98.9 months (5.5–259.7), there were 4 relapses (4.5% 4/89 cases), 2 for invasive and 2 for borderline. Only one of four recurrences died of the disease. 5-year disease free survival was 94.7% and 5-year overall survival rate was 95.2%.

Conclusion(s): Borderline ovary tumor had a favorable prognosis. Fertility saving surgery may be safe and beneficial to young women who desire to preserve fertility.

P-46 Body Mass Index change during Chemotherapy and prognosis in advanced ovarian cancer

Jae Yun Song, MD, PhD¹, Jae Kwan Lee, MD, PhD¹, Nak Woo Lee, MD, PhD¹, Dong Han Bae, MD, PhD², Kyu Wan Lee, MD, PhD¹ Department of Obstetrics and Gynecology, Korea University College of Medicine, Seoul, Korea¹, Department of Obstetrics and Gynecology, Soon Chun Hyang University College of Medicine, Cheonan, Korea²

Purpose of the study: To investigate body mass index (BMI) changes during chemotherapy for advanced ovarian cancer patients and to the association with survivals.

<u>Method(s)</u>: The medical records of the seventy patients who were treated by ovarian cancer from 1996 to 2007 at Korea University Hospital were reviewed retrospectively. After diagnosis and cytoreductive operation, body weight and height of patients were measured before first cycle chemotherapy and also after finishing sixth chemotherapy. Both pre-chemotherapy and post-chemotherapy BMI which was corresponded with WHO Asia-Pacific Guidelines were analyzed. Overall survivals according to the BMI, BMI change and body weight change were estimated by Kaplan-Meier.

<u>**Result(s)**</u>: Body weight and BMI were increased from 55.16kg to 56.83kg (p<0.05) and 23.26 to 23.95 (p<0.05). Prechemotherpy BMI was not correlated with survival (p=0.758). On post-chemotherapy BMI, overweight patients have improved survivals than ideal weight (p=0.043) and have a trend than overweight (p=0.097). There was an improved survival in no BMI change (-1 < <+1) patients than decreased (<-1) or increased (<+1) BMI patients (p=0.047).

Conclusion(s): Body weight and BMI are increased during chemotherapy. Minimal BMI change has improved survival but post-chemotherapy overweight has a trend to improved survival.

P-47 Treatment of advanced ovarian cancer (retrospective analyses)

Madina Kairbayeva, MD², V. Kuznetsov, MD¹, S. Nikogosyan¹

Russian N.Blokhin's Cancer Center, Moscow, Russia¹, Kazakh Medical University, Almaty, Kazakhstan²

Purpose of the study: To made retrospective analyses of treatment peculiarities of advanced ovarian cancer.

<u>Method(s)</u>: Evaluation of treatment results performed on data received from 271 patients with advanced ovarian cancer treated in gynecologic oncology department of Kazakh Institute of Oncology and N.Blokhin's Cancer Center during 1998–2002. Clinical assessments were made according to current recommendation. Sequence of treatment was defined by patient's age, somatic status and disease signs.

<u>Result(s)</u>: 14 patients had FIGO stage IIIa IIIb disease, 165 patients – IIIc, and 92 patients stage IV. Most common types of tumors were serous, endometrioid carcinomas – 213 and 23 cases respectively. Other types of tumor were mucinous (5), clear cell (5), germ cell (4), and others. Most common tumor grades were low and moderately differentiated tumors.

Most part of patients underwent combined-modality treatment (n=250). All patients underwent primary cytoreductive surgery which was complete in 19 cases, optimal in 51 and non-optimal in 184 patients accordingly. Typical surgery in these patients was total abdominal hysterectomy with omentectomy. In some cases we also performed appendectomy (n=10), hemicolectomy (n=4), small bowel resection, splenectomy. Staging laparotomy took place in 9 cases.

Chemotherapy as single treatment modality was given to 17 patients because of somatically inoperable conditions. Chemotherapy was not performed in 4 cases after cytoreductive surgery due to severe complications. As part of combined modality therapy all other patients underwent chemotherapy. Most common available chemo regimen in that time was CP (n=157), CAP (n=70), TP (n=40).

<u>Conclusion(s)</u>: among advanced ovarian cancer patients most common was stage IIIc disease (61%). The first common cancer type was serous cancers (84%). Surgery as the first treatment modality performed in most part of cases (73%), Chemotherapy as primary treatment was started in 24.8% of cases. most common chemo regimen was CP. Since that time we accepted new treatment guidelines, we broaden indications for extended surgery, LND and first line chemo regimens available in most regions of country.

P-48 Selection of the Optimal Bowel Surgery Between Low Anterior Resection With Primary Anastomosis and Hartmann's Procedure in Advanced Primary or Recurrent Epithelial Ovarian Cancer

Hee Seung Kim¹, Jae Weon Kim¹, Taek Sang Lee², Noh Hyun Park¹, Hyun Hoon Chung¹, Yong Sang Song¹, Soon–Beom Kang¹, Hyo Pyo Lee³

Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea¹, Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul National University Borame Hospital, Seoul, Korea², Department of Obstetrics and Gynecology, Konkuk University Hospital, Seoul, Korea³

Purpose of the study: We compared the efficacy between low anterior resection with primary anastomosis (LARA) and Hartmann's procedure (HP) in advanced primary or recurrent epithelial ovarian cancer (EOC).

<u>Method(s)</u>: We reviewed medical records of 61 patients with advanced primary or recurrent EOC who underwent LARA or HP between January 1998 and August 2008. In 37 patients with primary FIGO stage III-IV EOC, 22 and 15 received LARA and HP, whereas 10 and 14 underwent LARA and HP in 17 patients with recurrent EOC.

Result(s): The rectosigmoid obstruction after LARA was developed in 9.1% in advanced primary EOC and 10% in recurrent EOC. The stomafree rates were higher in LARA than in HP (90.9% vs. 0% in advanced primary EOC; 80% vs. 0% in recurrent EOC). Moreover, postoperative complications (rectovaginal fistula, leakage at the anastomotic sites, ileus, wound dehiscence, angina pectoris, acute renal failure, and reoperation) and surgical outcomes (time of operation, estimated blood loss, transfusion, postoperative hospitalization, and time to normal diet) were not different between LARA and HP. Progression-free (median, 20 vs. 20 months) and overall survivals (median, 70 vs. 36 months) in advanced primary EOC, and surgery-specific (median, 32 vs. 17 months) and overall survivals (median, 52 vs. 61 months) in recurrent EOC were not different between LARA and HP (p>0.05).

<u>Conclusion(s)</u>: Our findings demonstrate that LARA may have a higher stroma-free rate than HP with comparable postoperative complications, surgical outcomes and survival, suggesting that LARA is an acceptable procedure for bowel surgery in advanced primary or recurrent EOC.

P-49 Clinical study of Clear cell carcinoma of the ovary

Yoon Young Hwang, MD, Sang Geun Jung, MD, Sun Young Lee, MD, Chan Lee, MD, Seung Jo Kim Comprehensive Gynecologic Cancer Center, Bundang CHA General Hospital, Graduate School of Medicine, CHA University, Kyunngi-do, Korea

Purpose of the study: The aim of this study is to evaluate the clinical characteristics of the clear cell carcinoma of the ovary, and its responsiveness to postoperative platinum-based combination chemotherapy

<u>Method(s)</u>: Between March 1999 and May 2008, 15 patients with clear cell carcinoma of the ovary were identified at our institution. Data was retrospectively analyzed from available charts and pathologic reports.

<u>Result(s)</u>: Median age was 38.8 years (range 27–63 years). Tumors were 66.7% (10/15) stage I, 6.7% (1/15) stage II, 26.7% (4/15) stage III. All patients presented with a pelvic mass. All except 1 had optimal cytoreduction including total hysterectomy with bilateral salpingo-oophorectomy, omentectomy, bilateral para-aortic and pelvic lymph node dissection and multiple biopsy. One patient with stage III refused operation because of NYHA class III congestive heart failure. All patients received postoperative combination chemotherapy with platinum and paclitaxel. Recurrences occurred in 10% (1/10) stage I, 0% (0/1) stage II, 25% (1/4) stage III. With a median follow up duration of 32 months (range 2–86 months), 90% (9/10) stage I patients are alive without evidence of disease, while 75% (3/4) stage III patients were alive with cancer.

<u>Conclusion(s)</u>: Our data suggest that women with clear cell ovarian carcinomas frequently present at early stage and the survival rate was similar to that of other epithelial origin ovarian cancers.

P-50 Study of podoplanin expression and its biological characteristics in clear cell adenocarcinoma of ovary

Shuko Oe, MD, Kiyoshi Hasegawa, MD, Yukito Minami, MD, Yutaka Torii, MD, Rina Kato, MD, Shinichi Komiyama, MD, Yasuhiro Udagawa, Pr

Department of obstetrics and gynecology, Fujita Health University School of Medicine, Toyoake, Japan

Purpose of the study: Recently, podoplanin used as marker for lymphatic vessels or malignant mesothelioma. We reported that podoplanin immunoreactivity was observed in epithelial ovarian cancers and significantly stronger expressed on clear cell adenocarcinoma (CCC) than other histological types. We have also confirmed that inversed significant correlation between podoplanin expression and Ki–67 staining in CCC. In this study, we investigated the biological characteristics of podoplanin expression on CCC. Method(s): 1) We established a podoplanin gene transfected CCC cell line, designated RMG–1podo, derived from RMG–1, which did not express podoplanin. 2) We investigated the differences of cell proliferation, invasion capability and the sensitivity to anti-cancer drugs between both cell lines. The cell proliferation was examined by growth curve, invasion capability by Matrigel invasion assay, and the sensitivity to anti-cancer drugs, paclitaxel, SN–38, carboplatin and cisplatin by MTT assay. 3) Then, we transplanted both cell lines to nude mice intraperitoneally and compared transplanted tumor weight and immunoreactivity of Ki–67, PCNA, p53, p21, p27 and cyclin D1 for transplanted tumors of both cell lines.

Result(s): 1) There was no difference in doubling time and invasion capability between podoplanin -transfected RMG-1 cells, RMG-1podo and non-trasfected RMG-1 cells. However, RMG-1podo showed noteworthy lower sensitivity to pacitaxel and carboplatin than those of RMG-1. 2) There was no difference in transplanted tumor weight between RMG-1podo (0.70±0.35gr) and RMG-1 (1.02±0.16gr) (p=0.357). 3) Although, there were no morphological changes in both transplanted tumors by H&E staining, RMG-1podo transplanted tumor was revealed significantly decreased expression of Ki-67, PCNA than RMG-1 transplanted tumor. Moreover, RMG-1podo transplanted tumor was revealed significantly decreased expression p27. There were no differences in expression of p53 and p21 in both tumors.

<u>Conclusion(s)</u>: We confirmed that upregulation of podoplanin in CCC cells showed inhibitory effect on cell cycle in *vivo*, and chemoresistance in *vitro*. It was reported that CCC showed lower cell proliferation compared to other histological types, so CCC had chemoresistance to cisplatin–based chemotherapy. These findings suggested the possibility that podoplanin was related with cell proliferation and chemoresistance in CCC. Further investigation is needed to clarify the relationship between podoplanin expression and the biological characteristics of CCC.

P-51 Predictive parameters of mortality in patients with epithelial ovarian carcinoma

Jae Wook Kim¹, Sunghoon Kim², Bo Sung Yoon², Young Tae Kim², Jae Hoon Kim², Sang Wun Kim² Kwandong University College of Medicine, Myongji Hospital, Goyang-si, Korea¹, Yonsei University College of Medicine, Seoul, Korea²

Purpose of the study: Epithelial ovarian carcinoma is known for the poor prognosis since most of the patients are diagnosed with advanced stages. Various prognostic factors have been studied extensively, but characteristics associated with mortality of ovarian cancer patients are not clearly elucidated. Therefore, this study was conducted to define predictive parameters of mortality in ovarian cancer patients.

<u>Method(s)</u>: Data were collected from 399 patients who were diagnosed for epithelial ovarian cancer from Jan 1990 to Dec 2003. Of these patients, 255 women with thorough follow up medical records were included in the analysis. Probable predictive parameters of mortality, such as age, stage, parity, cell type, preoperative mass size, presence of ascites, residual volume, preoperative serum CA125 level, and DNA flow cytometry were evaluated and differences in these parameters between the decreased and survivors were analyzed. Statistical analysis was performed by chi-square ad multiple logistic regression analysis. The survival curves were obtained by the Kaplan–Meier method using SPSS version 12.0.

<u>Result(s)</u>: Of 255 study subjects, 84 patients (33%) were the decreased, and the mean overall survival was 63 ± 102.86 months, and mean disease free survival 43 ± 92.66 months. The statistically significant parameters associated with mortality were age (p=0.015), stage, presence of ascites, residual volume and preoperative serum CA-125 level (all p<0.001). In multivariate analysis, the powerful indicators predicting the mortality were age and the presence of ascites (odds ratio: 3.43, 2.51; p-value: 0.020, 0.034). And stage, cell type, presence of ascites, residual volume and preoperative serum CA-125 level were also the statistically significant factors predicting the recurrence in ovarian carcinoma. Among them, stage and the presence of ascites were the most predictive parameters of the recurrence of epithelial ovarian carcinoma (odds ratio: 2.69, 2.71; p-value: 0.031, 0.026).

<u>Conclusion(s)</u>: The presence of ascites was the most predictive indicator of both mortality and recurrence in epithelial ovarian cancer patients and this factor also has significant impact on the overall and disease free survival. Future studies regarding the effects of ascites volumes on mortality and survival of ovarian cancer patients should be encouraging.

P-52 Claudin-7 Inhibition Promotes Chemosensitivity in Epithelial Ovarian Carcinoma

Chul Jung Kim, Yoo-Young Lee, Chel Hun Choi, Tae-Joong Kim, Byoung-Gie Kim, Jeong-Won Lee, Duk-Soo Bae Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Purpose of the study: Claudin proteins are tight junction formation and function and they have been shown to be expressed differently in various cancers. The purposes of this study are to evaluate the expression of claudin-7 (CLDN-7) and its potential as a therapeutic target in epithelial ovarian carcinomas.

<u>Method(s)</u>: CLDN-7 expression was evaluated at the RNA level in fresh frozen ovarian carcinoma tissues by real-time quantitative reverse transcriptase polymerase chain reaction (RT-PCR). In addition, CLDN-7 expression was evaluated by immunohistochemistry in 45 formalin-fixed, paraffin-embedded ovarian tissues; 12 normal ovarian specimens; 33 epithelial ovarian carcinomas. To evaluate whether CLDN-7 inhibition can promote chemosensitivity in human ovarian cancer cells, we performed transfection with CLDN-7 siRNA and cisplatin in 2774 and HeyA8 cell *in vitro*

<u>Result(s)</u>: Real-time quantitative RT-PCR revealed that CLDN-7 expressions in epithelial ovarian carcinoma was significantly up-regulated compared with normal ovarian tissue (P<0.001). Moreover, immunohistochemical analysis showed that CLDN-7 expression was moderate to strong in all of epithelial ovarian carcinomas but there was no expression in normal ovarian epithelium. By siRNA-mediated down-regulation of CLDN-7, we showed that cisplatin promote cytotoxicity in 2774 and HeyA8 cells compared to control (P<0.05 in both cells).

<u>Conclusion(s)</u>: This study demonstrates that CLDN-7 expression remarkably increased in epithelial ovarian carcinoma compared with normal ovarian tissues and the combination of CLDN-7 inhibition by specific siRNA and cisplatin showed significant reduction in cell growth. These results indicate that CLDN-7 might be a molecular target to promote chemosensitivity for ovarian cancer therapy.

P-53 Frequent inactivation of *hSRBC* in ovarian cancers by promoter CpG island hypermethylation

Seon-Kyung Lee, Seo-Yun Tong, Kyung-Do KI, Jong-Min Lee

Department of Obstetrics and gynecology, East-West Neo Medical Center, Kyung Hee University, Seoul, Korea

Purpose of the study: Mutation and altered expression of *hSRBC*, a novel tumor suppressor located at 11p15, have been observed in several human cancers. To explore the implication of *hSRBC* abnormality in ovarian tumorigenesis, we investigated expression and mutation of *hSRBC* in cancer cell lines and primary carcinoma tissues

<u>Method(s)</u>: hSRBC expression was characterized by polymerase chain reaction (PCR) analysis. Promoter CG dinucleotide (CpG) site methylation was determined using methylation specific PCR and bisulfite sequencing.

<u>Result(s)</u>: Expression of *hSRBC* transcript was easily detectable in all normal tissues we examined, but 50% (2 of 4) of cancer cell lines and 41% (9 of 22) of primary carcinomas exhibited undetectable or substantially decreased expression. While genomic deletion or somatic mutations of the gene was not identified, its expression was reactivated in tumor cells by 5-aza-2'-deoxycytidine treatment, suggesting epigenetic inactivation of the gene in tumors. Promoter methylation was detected in all 9 tumors with low expression but in only 1 of 13 (7.7%) tumors with normal expression. Bisulfite DNA sequencing analysis of 23 CpG sites within the promoter region revealed that the CpG sites are highly methylated in low-expressing tumors. In addition, promoter CpG sites methylation status showed a tight association with gene expression level.

<u>Conclusion(s)</u>: Our data demonstrate that epigenetic inactivation of *hSRBC* due to aberrant promoter hypermethylation is a common event and might be implicated in human ovarian tumorigenesis.

P-54 Identification of Stress-induced phosphoprotein-1 (STIP-1) as a Diagnostic and Therapeutic Biomarker for Ovarian Cancer

Jae-hoon Kim, MD

Department of Obstetrics and Gynecology, Gangnam Severance Hospital, Yonsei, University College of Medicine, Seoul, Korea

<u>Purpose of the study</u>: To investigate new diagnostic and therapeutic biomarker candidate for ovarian cancer using immunoprecipitated tumor antigen

<u>Method(s)</u>: We used two-dimensional differential gel eletrophoresis analysis of immunoprecipitated tumor antigens (2D–DITA) to identify autoantibodies against relevant tumor antigens in the serum of 14 ovarian cancer patients pre- and post-operatively. Low levels of autoantibodies against tumor antigens in the postoperative serum samples compared with the preoperative serum samples should pull down smaller amount of tumor-associated antigens (TAAs). The one spot (TAA) that showed the highest differential signals was identified by decyder biological variation analysis. To validate the data with our 2D–DITA technology, we used quantitative real-time quantitative reverse transcription polymerase chain reaction (RT–PCR), immunohistochemistry (IHC). Plasma level of selected biomarker candidate was measured by an enzyme–linked immunosorbent assay (ELISA). Ovarian cancer cell lines were transfected with the small interfering RNA (siRNA) and the effect of cell proliferation was assessed.

<u>Result(s)</u>: The one spot identified stress-induced phosphoprotein-1 (STIP-1) was highly expressed in the preoperative serum samples compared with the postoperative serum samples with statistical significance (p<0.05). Real-time RT-PCR and IHC studies revealed that mRNA and protein of STIP-1 were highly expressed in ovarian cancer but nearly absent in normal cell-lines and tissues (p<0.05). Plasma STIP-1 level was significantly higher in ovarian cancer patient compared with the healthy control group (p=0.005). Knockdown of STIP-1 with anti-STIP-1 siRNA resulted in a significant reduction of cell proliferation after day5.

<u>Conclusion(s)</u>: STIP-1 is a potentially useful diagnostic and therapeutic marker for ovarian cancer. Further research assessing their putative clinical usefulness would be worthwhile.

P-55 The evaluation of the immune state by using the hierarchical clustering of tumor-infiltrating immune cells in ovarian cancers

Junzo Hamanishi, MD, PhD, Masaki Mandai, MD, PhD, Noriomi Matsumura, MD, PhD, Tsukasa Baba, MD, PhD, Ken Yamaguchi, MD, PhD, Ikuo Konishi, MD, PhD

Department of Gynecology and Obstetrics, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Purpose of the study: Tumors battle with or escape from host immune cells at the tumor microenvironment. The aim of this study is to the way to evaluate local immune states of human ovarian cancers by the hierarchical clustering of the tumor-infiltrating immune cells and immunosuppressive factors and the subgroups.

<u>Method(s)</u>: Using immunohistochemical staining of paraffin enbedded 70 ovarian cancer specimens, the numbers of CD4+, CD8+, CD57+, CD1a+, foxp3+, or PD-1+ cells infiltrating were counted, and the intensity of seven immunosuppressive factors such as PD-L1, PD-L2, COX1, COX2, TGFb1 (11immunological factors) were replaced with neumeral value. Hierarchical clustering was used to analyze these parameters at one time.

<u>Result(s)</u>: We found 4 with high CD4+cell, CD8+ cell and CD1a+, ell density was better than other clusters.clusters in 70 tumor samples from the patients. Cluster1 had a peculiar findings such as a large number of many kinds of immune cells without any immunosuppressive factors. The overall survival of cluster 1

<u>Conclusion(s)</u>: In conclusion, hierarchical clustering of tumor-infiltrating immune cells and immunosuppressive factors indicated best prognostic subgroup of ovarian cancer and suggested thatimmunosuppressive factors may influence the pattern of tumor-infiltrating immune cells and prognosis in ovarian cancer.

P-56 Promoter hypermethylation of *TGFBI* in epithelial ovarian cancer

Sokbom Kang, MD, Myung-Chul Lim, MD, Sang-Soo Seo, MD, Seung-Myun Dong, MD, Sang-Yoon Park, MD Research Institute and Hospital, National Cancer Center, Goyang, Korea

Purpose of the study: Ovarian cancer is the most lethal gynecologic cancer. Accumulating evidence of epigenetic inactivation in tumor suppressor genes led us to conduct a comprehensive screen to identify novel methylated genes in ovarian cancers using pharmacologic unmasking and genome-wide differential methylation analysis.

<u>Method(s)</u>: Two ovarian cancer cells (OVCAR-3, ES-2) that showed synergistic growth inhibition by 5-aza-dC and cisplatin. After treating with 5-aza-dC, differential expression profile was compared using microarray containing 38,500 genes. Reactivation of candidate genes and its promoter methylation was validated by realtime RT-PCR, MS-PCR and bisulfite sequencing. Methylation status was tested using MS-PCR in 56 patients with epithelial ovarian cancer and compared with the 38 normal ovarian tissues.

<u>Result(s)</u>: We identified 103 candidate genes which were reactivated by 5–aza–dC treatment. Among those genes, SFN and *TGFBI* were genes that were reactivated commonly in both cells. Since *SFN* was a well known methylated marker, we validated silencing and reactivation of *TGFBI* by 5–aza–dC using real–time RT–PCR. Bisulfite sequencing revealed complete promoter methylation in ES–2 and partial methylation in OVCAR–3. *TGFBI* methylation was observed in 23 out of 38 (60.5%) cases of ovarian cancer, while it is observed in none of normal ovarian tissues (*P*=0.001) and 5 out of 18 (27.8%) cases of borderline tumor (*P*=0.044). *TGFBI* methylation was not found in normal ovarian tissues. However, methylation of *TGFBI* was not associated with any clinicopathologic variables or survival outcomes.

Conclusion(s): Our results confirm that *TGFBI* is frequently methylated in ovarian cancer. Its methylation can be used as a novel epigenetic biomarker in discriminating ovarian cancer from non–cancer or borderline tumors.

P-57 The development and application of MAb Chi–Cx–99 on cancer diagnosis and therapy

Chiou-Chung Yuan, MD

Department of Obstetrics and Gynecology, Branch for Women & Children, Taipei City Hospital, National Yang-Ming University, Taipei, Taiwan

Purpose of the study: Cytokeratin 19 (CK19) is a constitutive cytoskeleton protein express in most epithelial cells. In tumorigenesis processes, expression of CK19 is up-regulated. In 1992, we developed a mouse monoclonal antibody (MAb) named Cx-99 which against CK19 epitopes which is distinct from other commercially available CK19 antibody. MAb Cx-99 can be applied in detecting numerous kinds of cancers tissues like cervical, ovarian, breast, and lung. However, Cx-99 is mouse monoclonal antibody which will induce a human anti-mouse antibody (HAMA) reaction and be restricted in application of immunotherapy like antibody dependent cellular cytotoxicity (ADCC) or targeting therapy. Therefore, we proceed to develop a chimeric antibody which possesses human constant region and mouse variable region against CK19.

<u>Method(s)</u>: Molecular cloning, transfectoma cell culture, protein purification, immunohistochemical staining, radioisotope labeling, scintigraphy, ⁵¹ Cr uptake for cytotoxicity test, NK cells isolation and activity induction, and ADCC were performed in this study.

<u>Result(s)</u>: MAb-Chi-Cx-99 also possesses a good binding affinity to CK19 in comparison with MAb Cx-99. Using MAb Chi-Cx-99 to perform immunohistochemical staining, we found positive response in cervical, ovarian, breast, and lung cancer tissues. After labeling with ¹³¹I and performing scintigraphy, we also found that ¹³¹I-labeled-Chi-Cx-99 could target xenografted cervical cancer specifically. In an ADCC experiment, ovarian cancer cell line TOV-21G cells and ES2 cells which express high and low CK19 respectively were adopted. Results revealed that PBMC-derived natural killer (NK) cells kill TOV-21G more effective than ES2 cells in presence of 100µg/ml of MAb Chi-Cx-99. In an E/T ratio of 5/1, pretreatment of MAb Chi-Cx-99 in a concentration of 100µg/ml, cytotoxicity of NK cells to TOV-21G was accelerated from 57.01% to 80.35%.

<u>Conclusion(s)</u>: These results demonstrate that the mouse-human chimeric antibody Chi–Cx–99 against fragments of cytokeratin 19 expressed on the cancer cells surface has a highly potential in applications of cancer diagnosis and therapy.

P-58 Neuroprotective effects of 17beta-estradiol in Sk-N SH neuroblastoma cells

Yongil Kwon, MD, Ph.D.

Kangdong Sacred Heart Hospital, Hallym University School of Medicine, Seoul, Korea

Purpose of the study: The present study was performed to evaluate the neuroprotective effects of Estradiol *in vitro* and *in vivo* experiments.

Estrogens have long been recognizes as antioxidants and recent studies have showed that Estrogens are also potent neuroprotective agents, but the mechanisms underlying protection by estrogen are not clear.

<u>Method(s)</u>: We assessed the neuroprotective effects of estrogens in human neuroblastoma SK–N–SH cells and the potential mechanisms involved in this protection.

<u>Result(s)</u>: The Estradiol, one of the Estrogens, is hormone that generates new protein synthesis promotion and cellular proliferation function. In addition, Estradiol exerts the protective effects by attenuating ATP depletion, generation of ROS (Reactive Oxygen Species) induced by mitochondrial calcium overloading.

In conclusion, Estradiol exerts protective effects against oxidative stress by subsequently preserving Ca^{2} + homeostasis, mitochondrial membrane potential, and ATP levels.

<u>Conclusion(s)</u>: Therefore, we investigated whether 17β -E₂ had prevent effect the SK-N-SH human neuroblastoma cell viability and valuable dose.

P-59 Activated local immunity by CCL19-transduced embryonic endothelial progenitor cells suppresses metastasis of murine ovarian cancer

Masaki Mandai, MD, PhD, Junzo Hamanishi, MD, PhD, Noriomi Matsumura, MD, PhD, Tsukasa Baba, MD, PhD, Ken Yamaguchi, MD, PhD, Ikuo Konishi, MD, PhD

Department of Gynecology and Obstetrics, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Purpose of the study: Although tumor microenvironments plays a key role in successful tumor immunotherapy, effective manipulation of local immunity is difficult due to the lack of an appropriate target system. Recently, iIt is well known that bone marrow-derived endothelial progenitor cells (EPCs) are actively recruited during tumor angiogenesis.

<u>Method(s)</u>: The eEPCs were retrovirally transduced with the mouse CC chemokine ligand 19 (CCL19) gene, a lymphocytemigrating chemokine. First, tThe mouse ovarian cancer cell line OV2944–HM–1 (HM–1) was inoculated subcutaneously into B6C3F1 mice, along with CCL19–tranduced eEPCs (eEPC–CCL19), and resulting in immunological activity as well as and tumor–inhibitory effects was evaluated.

<u>Result(s)</u>: In the simultaneous subcutaneous injection model, compared with the control group, mice injected with CCL19tranfected eEPCs exhibited tumor regression, accompanied by increased tumor–infiltrating CD8+ lymphocytes. In the lung metastatic model also, there were significantly fewer metastatic nodules in the lungs of mice injected with CCL19–tranfected eEPCs than in the control group.

<u>Conclusion(s)</u>: Systemic delivery of an immune-activating signal using EPCs can alter the tumor immune microenvironment and leads to a therapeutic effect, which may provide a novel strategy for targeting multiple metastases of various malignancies.

P-60 Simultaneous detection of proliferation, apoptosis, invasive ability, and cytoskeletal organization in gynecological cancer cells by nanodot arrays device

Yao-Ching Hung, MD, PhD¹, W-C Wu, MD¹, H-A Pan, MS², S-M Tai, MS², G-S Huang, PhD²

Department of Obstetrics and Gynecology, China Medical University and Hospital, Taichung, Taiwan¹, Institute of Nanotechnology, National Chiao Tung University, Hsin–Chu, Taiwan²

Purpose of the study: Extracellular matrix contains structures from micro-scale down to nano-scale. We hypothesized that cells respond to both micro-structure and nano-structure. The aim is to apply nano-surface device to distinguish gynecological cancer cell lines by their invasive potentials. We have fabricated a nanodevice composed of a matrix of nine nanodot arrays with various dot sizes ranging from a flat surface to 10-nm, 50-nm, 100-nm, and 200-nm arrays.

<u>Method(s)</u>: Cervical cancer cell lines (HELA, C33A), ovarian cancer cell lines (ES2, PA-1, TOV-112D, TOV-21G), MG63, and NIH-3T3 cells were seeded onto the device and cultured for three days. Cell density was measured to examine the proliferation of cells, and scanning electron microscopy (SEM) was performed to assess morphological changes in cells. To evaluate cell adhesion and cytoskeletal reorganization, immunostaining specific to vinculin and actin filaments was performed.

<u>Result(s)</u>: The scores for cell proliferation, morphology, distribution of focal adhesions, and cytoskeletal reorganization were obtained. We were able to distinguish between the invasive ability of HELA versus later-staged C33A cells. Ovarian cancer cell lines (ES2, PA-1, TOV-112D, and TOV-21G) also exhibited differential growth parameters that are associated with cell type, grade, and stage. Modulation of the growth of MG63 was also achieved.

<u>Conclusion(s)</u>: We have established a platform that can be used to assess multiple parameters of cell growth. A simplified fabrication process ensures mass production and lowers cost. According to our results, the device is capable of distinguishing among gynecological cancer cell lines of various stages and also provides basic design parameters for artificial implants. Our device will serve as a convenient and fast tool for tissue engineering and cancer treatment.

P-61 Size-dependent immune properties of gold nanoparticles as a drug (vaccine) targeting carrier in nanomedicine-elicited by synthetic Foot-and-mouth disease virus peptide

Yao-Ching Hung, MD, PhD¹, L-M Chen, MD¹, Y-S Chen, PhD², W-H Lin, MS², G-S Huang, PhD²

Department of Obstetrics and Gynecology, China Medical University and Hospital, Taichung, Taiwan¹, Institute of Nanotechnology, National Chiao Tung University, Hsin–Chu, Taiwan²

Purpose of the study: To elicit the size-dependent immune properties of gold nanoparticles (GNPs) for the application of drug (vaccine) carrier targeting cancer tissues, a synthetic peptide corresponding to Foot-and-mouth disease virus (FMDV) viral proteins was conjugated to GNPs ranging from 2–50nm in diameter (2nm, 5nm, 8nm, 12nm, 17nm, 37nm, and 50nm). An extra cysteine was added to the C-terminus of the FMDV peptide (pFMDV), to ensure maximum conjugation.

<u>Method(s)</u>: The pFMDV-GNP conjugates were injected into BALB/C mice. Immunization with pFMDV-keyhole limpet hemocyanin (KLH) conjugate was performed as the control. Blood was withdrawn from mice on weeks 4, 6, 8, and 10, and antibody titers against pFMDV and carriers were obtained. For pFMDV-GNP immunization, specific binding against peptide was detected in the sera of mice injected with 2 nm, 5nm, 8nm, 12nm, and 17nm GNP conjugates.

Result(s): Maximum binding occurred with GNPs of sizes between 8nm to 17nm. The pFMDV–GNPs induced a 3–fold increase in antibody response compared to pFMDV–KLH. In particular, all sera exhibited undetectable binding against GNP, while antisera of pFMDV–KLH presented high levels of binding activity against KLH. The uptake of pFMDV–GNP in spleen was examined by ICP–MS and TEM.

<u>Conclusion(s)</u>: The amount of GNP accumulated in the spleen correlated to the immune response induced by pFMDV-GNP. In conclusion, we demonstrated the size-dependent immunogenic properties of pFMDV-GNP conjugates. GNPs ranging from 8nm to 17nm promotes the most intense immune response, thus should be avoided if used as drug (vaccine) carrier. GNPs of sizes outside of this zone will be potential drug (vaccine) carriers in the application of nanomedicine.

P-62 Comparison of results of treatment of patients with GTN referred to a trophoblastic disease center after failure of treatment elsewhere and primarily treated at trophoblastic disease center

Seung Jo Kim, MD, Sang Geun Jung, MD, Sun Young Lee, MD, Chan Lee, MD, Yoon Young Hwang, MD

Comprehensive Gynecologic Cancer Center, Bundang CHA General Hospital, Graduate School of Medicine, CHA University, Kyunngi-do, Korea

Purpose of the study: To review the results of treatment of patients with GTN who were transferred to our trophoblastic disease center after failure of primary therapy elsewhere and compare its results with treatment results of patients with GTN treated primarily at our center

<u>Method(s)</u>: Total sixty-nine patients with GTN were treated at trophoblastic disease center, Bundang CHA General Hospital, CHA university from 1995 to 2005. We divided all patients into two groups by institute of primary treatment. One is patients groups referred to our center after failure of primary therapy at other institutes and the other is patients who treated primarily at our center. We analyzed clinical characteristics and compare results of treatment of two groups retrospectively.

<u>Result(s)</u>: Total one hundred sixty-eight patients of GTD were treated at our trohphoblastic center and among these patients 69 patients are diagnosed with GTN and forty-seven patients (68.1%) of total 69 patients with GTN were referred to our trophoblastic disease center after failure of primary treatment. There were 4 dead patients who were treated at our center after failure of primary treatment at other institutes. The most common causes of treatment failure prompting referral to our center were inappropriate dose or schedule of chemotherapy, the presence of widely metastatic disease and absence of management of high risk hydatidiform mole.

<u>Conclusion(s)</u>: Overall survival was 91.5% (43/47) for patients with GTN who failed treatment before referral to our trophoblastic diseases center, compared to 100% for patients with GTN treated primarily at our center (p<0.05).

P-63 Plasma Selenium Concentrations in the Gynecologic Cancer Patients: Prelininary study for the supplemental nutrition therapy

Soo Hyun Kim, MD, Sang Geun Jung, MD, Sun Young Lee, MD, Chan Lee, MD, Yoon Young Hwang, MD, Seung Jo Kim, MD Comprehensive Gynecologic Cancer Center, Bundang CHA General Hospital, Graduate School of Medicine, CHA University, Kyunngi-do, Korea

Purpose of the study: Selenium is an essential micronutrient for human and animals. The role of selenium has been largely attributed to its presence in selenoproteins as the 21st amino acid, selenocysteine. Selenoproteins has been believed to be close linked with cancer and carcinogenesis, because there are numerous epidemiological reports on inverse correlation between selenium intake and occurrence of cancer risk.

<u>Method(s)</u>: A total of 136 Korean women aged 21~75 years were included. All patients took blood sampling before and after treatment and during follow up in the different group of cancer patients. (benign: 87cases, premalignant: 11cases, early-stage cancer: 15cases, advanced stage cancer: 12cases, recurrent: 11cases). Selenium concentrations were measured by Atomic Absorption Spectrometer (AAS) method using Analyst [™] 800 (Perkin-Elmer, Germany)

<u>**Result(s)**</u>: Selenium values were 93.9 \pm 14.1 (benign group), 92.6 \pm 5.9 (premalignant group), 89.2 \pm 14.4 (early stage group), 80.7 \pm 14.8 (advanced stage group) and 73.7 \pm 10.5 (recurrent group) respectively. No major differences were detected between benign and premalignant group. However, a significant interaction between benign and advanced stage group especially, recurrent group of cancer patients (P=0.0013)

<u>Conclusion(s)</u>: Since selenoproteins have biological functions in oxidoreductions, redox signaling, antioxidants defense or immune responses, our results suggested that selenium may not only be involved in incidence but may also have a role in progression of the cancer. Further studies will be necessary more extensively in the future.

P-64 The Prevalence and Risk Factors of Lower Limb Lymphedema in the Patients with Gynecologic Cancer

Sung Han Kim, M.D., Tae-Hwa Lee, M.D.

Department of Obstetrics and Gynecology, Kosin University Collge of Medicine, Busan, Korea

Purpose of the study:

Objective: To identify the prevalence and risk factors for lower limb lymphedema in the patients after gynecologic neoplasms treatment in Korea.

Method: We retrospectively reviewed the medical records and interviewed 242 gynecologic neoplasms patients who have managed surgically and medically over a 4 year period between January 2003 and December 2006. We identified the patients with lower limb lymphedema as described by the medical records or reported by the interviews. We obtained demographic characteristics, other medical history, cancer type, stage of cancer, lymph node dissection, chemotherapy, radiotherapy, hormone therapy and laboratory findings. Multiple logistic regression analysis was done to evaluate the risk factors for lower limb lymphedema.

Results: Forty eight (19.8%) patients out of two hundred forty two had lower limb lymphedema. Those patients with lower limb lymphedema had a higher body mass index, radiotherapy history, chemotherapy history and lymph node dissection history. Multivariate analysis revealed that body mass index, radiotherapy and lymph node dissection were independently risk factors for lower limb lymphedema after gynecologic neoplasms treatment.

Conclusion: The patients who had radiotherapy, body mass index greater than 25 or lymph node dissection must be considered as potential candidates to have lower limb lymphedema in the patients after gynecologic neoplasms treatment. Therefore, these patients should be informed during the follow-up period about this morbidity, the preventive measures, and the treatments.

Key Words: Lymphedema, Gynecologic neoplasms, Risk factor

P-65 Ovarian sclerosing stromal tumor associated with elevated CA125 and Meigs' syndrome: case report

Wei-Shiu Chen, MD, Jui-Chang Hsu, MD, Horng-Der Tsai, MD

Department of Obstetrics and Gynecology, Changhua Christian Hospital, Changhua, Taiwan

Introduction: Sclerosing stromal tumor (SST) is a rare benign ovarian neoplasm with prevalence of less than 5% of sexcord stromal tumor. Meigs' syndrome is consisting of ovarian tumor of fibroma-thecoma group with ascites and hydrothorax that can be resolved by surgical removal of the tumor

<u>Case</u>: We present a 17-year-old female with initial symptoms of polymenorrhea, progressive abdominal distension, poor appetite, weight gain and dyspnea. Much ascites, bilateral pleural effusion, pelvic mass measuring 16×14×10cm, and elevated CA125 of 4208.3U/mL were noted. Ovarian epithelial malignancy was highly suspected before operation. Diagnostic laparoscopy was performed first. Because of no diffuse peritoneal carcinomatosis, operative method was changed to laparotomy. Intra-operative histology of right adnexa showed benign stromal cell tumor. The permanent pathology revealed sclerosing stromal tumor of right ovary. The patient had uneventful postoperative recovery and very regular menstruation. **Conclusion(s):** In conclusion, SST is a rare benign tumor. Although the clinical findings of ovarian tumor, ascites, pleural

<u>conclusion(s)</u>: In conclusion, SST is a rare beingin tumor. Although the chinical initiality of ovarian tumor, asches, pieural effusion, and elevated CA125 is highly predictive of epithelial ovarian cancer, the possibility of Meigs'syndrome must always be considered. Minimal invasive surgery for biopsy and intraoperative histology are strongly suggested to prevent unnecessary treatment.

P-66 Ovarian fibroma presenting elevated CA 125 and malignant pleural effusion: case report

Lung-Yung Wong, MD, Jui-Chang Hsu, MD, Horng-Der Tsai, MD

Department of Obstetrics and Gynecology, Changhua Christian Hospital, Changhua, Taiwan

<u>Introduction</u>: Ovarian fibroma is a stromal tumor, which accounts for 4% of all ovarian tumor. Ovarian fibroma is almost always benign in nature. It may be associated with ascitis and pleural effusion. We report a case of ovarian fibroma who has the result of cytology of pleural effusion which showed adenocarcinoma and elevated CA-125.

<u>Case</u>: A case of 69 y/o female had large ovarian tumor with elevated CA 125 (181.9U/ml~589U/ml) for 7 years. A diagnosis of malignant ovarian tumor was made as the cytology of pleural effusion showed adenocarcinoma in year 2002 after general survey. One cycle of chemotherapy with Cisplatin was performed in the same year, which decreased CA 125 level from 400.6 U/ml to 181.9U/ml. She refused for further chemotherapy or the operation because of social reason in these 7 years. She had regular follow up at hematology outpatient department for palliative treatment only in these years. Progressively enlarged ovarian tumor found. She came to gynecology outpatient departement for help in this year because of complete uterine prolapse, voiding difficulty and constipation which were suspected causing by the compression of large ovarian tumor measuring $21 \times 18 \times 10$ cm. She finally agreed for the operation. The frozen section was performed during the operation and showed benign lesion. The histopathology result showed ovarian fibroma with cystic change.

<u>Conclusion</u>: Although the result of cytology showed malignancy, invasive surgery for biopsy and intraoperative histology are strongly suggested to confirm the diagnosis.

P-67 Tuberculosis in iliac lymph nodes complicating a case of invasive ductal carcinoma of breast

Lin Chao-po, MD

Chia-Yi Christian Hospital, Chia-yi, Taiwan

Purpose of the study: To present a case of breast cancer been complicated with pelvic lymphadenopathy which proved extrapulmonary tuberculosis.

Method(s): This 36 y/o female, G3P2A1, was a victim of invasive ductal carcinoma of right breast (pT2N2MX, stage III, ER (-) PR(-) Her2/neu 3+). She received right breast modified radical mastectomy in Mar 2008 and kept postoperative chemotherapy. She just recovered from Staphylococcal Port-A infection in Sep 2008. Unfortunately, she felt headache and intermittent high fever for days in Oct 2008. Empirical antibiotics were given for possible sepsis. However, no specific infectious focus was suspected. And the inflammation scan was also negative. The neck and abdomen CT scan did not reveal any evident recurrence except some suspicious lymphadenopathies in the para-aortic region and bilateral iliac chain to R/O metastases or gynecologic malignancy. However, the CT scan and ultrasonography and tumor marker survey did not show any abnormality.

<u>Result(s)</u>: The pelvic lymph node excision biopsy was performed. It proved extrapulmonary tuberculosis (pathology: extensive necrosis with scanty suspicious acid-fast(+) bacilli). She was then successfully treated with anti-tuberculous therapy of 9 months.

Conclusion(s): Extrapulmonary tuberculosis is not uncommon in people of impaired immunity. Its diagnosis necessitates a high index of suspicion. In case of treated cancer patients with lymadenopathies of unknown nature, pathological proof is mandatory.

P-68 Large cell neuroendocrine carcinoma of the uterine cervix: A report of a case with coexisting high grade cervical intraepithelial neoplasia and human papillomavirus 18

Jae-Whoan Koh, MD

Departments of Obstetrics and Gynecology, Seoul Paik Hospital, Inje University, Seoul, Korea

Purpose of the study: This study aimed to show the different immunophenotype and HPV integration profile between large cell neuroendocrine carcinoma (LCNEC) and cervical intraepithelial neoplasia (CIN) in the uterine cervix.

<u>Method(s)</u>: The 54 year old patient underwent a punch biopsy for exophytic cervical mass. The biopsy specimen was immunostained for chromogranin A, synaptophysin, carcinoembryonic antigen (CEA) and TTF-1, followed by microdissection of the LCNEC lesion against the CIN lesion under high field microscopy. Human papillomavirus (HPV) subtypes were detected in two separated tissues by nested polymerase chain reaction (PCR).

Result(s): The biopsy specimen was mainly composed of LCNEC which showed pleomorphic tumor cells with invasive, solid and trabecular growth patterns, frequent mitotic figures, and lymphatic invasions. The neoplastic cells were positive for chromogranin A, synaptophysin, CEA and TTF-1. The high grade CIN lesion was negative for these markers and positive for high molecular weight cytokeratin. Microscopically the LCNEC component extended beneath the CIN lesion as with questionable transitional foci. Separate PCR using microdissected tissue from each component demonstrated only HPV type 18 DNA in LCNEC component whereas both type 16 and 18 DNA in CIN component.

<u>Conclusion(s)</u>: TTF-1 expressed neuroendocrine carcinomas of the uterine cervix are very rare cervical neoplasms and LCNEC of the uterine cervix is aggressive malignancy. Polymerase chain reaction (PCR) using genomic DNA extracted from microdissected tissue demonstrated human papillomavirus (HPV) type 18 DNA in both the LCNEC and CIN lesions, whereas type 16 DNA in CIN lesion only. These immunohistochemical and PCR findings suggested that the LCNEC lesion was distinct from the CIN lesion, rather than divergent differentiation of CIN cells to neuroendocrine carcinoma cells.

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