Min Cheng **鄭敏**
(Y1)

Weekly Dose-Dense Paclitaxel and Tri-weekly Low-Dose Cisplatin: A Well-Tolerated and Effective Chemotherapeutic Regimen for First-Line Treatment of Advanced Ovarian, Fallopian Tube, and Primary Peritoneal Cancer

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BACKGROUD: A combination of cytoreductive surgery, either primary (PCS) or interval (ICS), and chemotherapy with platinum-paclitaxel regimen is the well accepted treatment for advanced-stage epithelial ovarian cancer (EOC), fallopian tube cancer (FTC), and primary peritoneal serous carcinoma (PPSC), but it is still uncertain whether a combination of dose-dense weekly paclitaxel and low-dose tri-weekly cisplatin is useful in the management of these patients.
METHODS: This is a single-arm, single-institution retrospective cohort study. We evaluated the outcomes of women with advanced-stage EOC, FTC, and PPSC treated with PCS and subsequent six cycles of dose-dense weekly paclitaxel (80 mg/m2) and low-dose tri-weekly cisplatin (20 mg/m2). The primary endpoint was PFS. The secondary endpoints were OS, overall response rate (ORR), clinical benefit rate (CBR) and safety.
RESULTS: Between January 2011 and December 2017, 32 women with International Federation of Gynecology and Obstetrics (FIGO) stage IIIC-IV EOC, FTC, and PPSC were enrolled. Optimal PCS was achieved in 63.5% of patients. The mean and median progression-free survival was 36.5 and 27.0 months, respectively (95% confidence interval [CI], 26.8-46.2, and 11.3-42.7 months respectively). The mean overall survival was 56.0 months (95% CI 43.9-68.1 months), and the median overall survival could not be obtained. The most common all-grade adverse events (AEs) were anemia (96.9%), neutropenia (50%), peripheral neuropathy (28.1%), nausea and vomiting (34.4%), and thrombocytopenia (15.6%). These AEs were predominantly grade1/2 and only a few patients were complicated by grade 3/4 neutropenia (21.9%) and anemia (6.3%), respectively. Multivariate analysis indicated that only suboptimal PCS was significantly correlated with a worse prognosis, resulting in an 11.6-fold increase in the odds of disease progression.
CONCLUSIONS: Our data suggests that dose-dense weekly paclitaxel (80 mg/m2) combined with low-dose tri-weekly cisplatin (20 mg/m2) is a potentially effective and highly tolerable front-line treatment in advanced EOC, FTC, and PPSC. Randomized trials comparing the outcome of this regimen and other standard therapy for FIGO IIIC-IV EOC, FTC and PPSC are warranted.

Hsiang-Chun Dong **董祥鈞**
(Y2)

Using deep learning with convolutional neural network approach to identify the invasion depth of endometrial cancer in myometrium using MR images

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Background: Myometrial invasion is a crucial factor in endometrial cancer prognosis. Discrepancy still exists between the pre-operative magnetic resonance imaging (MRI) staging and the post-operative pathological staging. We aimed to validate the accuracy of artificial intelligence (AI) for detecting the depth of myometrial invasion using deep learning (DL) techniques on MR images.

Methods: A total of 4896 slices from T2-weighted images (T2WI) and contrast-enhanced T1-weighted images (T1WI), along with radiology reports were obtained retrospectively for 72 patients diagnosed with surgico-pathological stage I endometrial carcinoma. Gynecologists stratified 33.3% (24 patients) of the MR images to a training set to train the DL model. Data from the remaining 48 patients (66.7%) were used to appraise the accuracy of the model, with subsequent interpretation of each case into stage IA or IB.

Results: Compared with the diagnostic accuracy of radiologists (77.8%), the depth of myometrial invasion was determined by the trained DL model (VGG11) with 79.2% accuracy in the test set with contrast-enhanced T1WI, and by the trained DL model (ResNet34) with 70.8% accuracy with T2WI. AI achieved the same image discrimination rate as that of radiologists. Diagnostic efficiency did not differ significantly between radiologists and AI for contrast-enhanced T1WI and T2WI ($p=0.856$ and $p=0.392$, respectively).

Conclusions: DL can play a pivotal role in evaluating the depth of myometrial invasion of endometrial cancer. Model selection and establishment are the keys to improve the performance of AI.

Keywords: Artificial Intelligence, Endometrial Neoplasms, Magnetic Resonance Imaging, Neoplasm Staging, Neural Networks (Computer).

Yu-Hsiang Shih 石宇翔
(Y3)

Long-term Outcomes and Toxicities after treating Intermediate- or High-Risk Cervical Cancer with Intensity-Modulated Radiation Therapy After Radical Hysterectomy

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Objectives: Patients with cervical cancer who have undergone radical hysterectomy can receive intensity-modulated radiation therapy (IMRT), either as an adjuvant therapy or as a primary treatment. The reported follow-up periods are typically short. This retrospective study evaluated the long-term outcomes and toxicities of adjuvant IMRT and brachytherapy with or without concurrent chemotherapy (CCRT) for treating patients with cervical cancer.

Methods: In total, 200 patients underwent radical hysterectomy for stage IB1 to IIB cervical cancer in our institute from January 2004 to December 2015. Patients with intermediate risk factors received adjuvant IMRT at a median dose of 50.4 Gy and those with high risk factors received adjuvant IMRT along with CCRT of cisplatin at a weekly dose of 30 mg/m2.

Results: At a median follow-up of 102 months, 21 patients with intermediate risk factors received adjuvant IMRT. The overall survival (OS) rates were 95.0% (3-year), 90% (5-year), and 90% (10-year). The progression-free survival (PFS) rates were 90.4% (3-year), 90.4% (5-year), and 90.4% (10-year). Another 21 patients with high risk factors received IMRT with CCRT. Their OS rate was 89.2% (3-year, 5-year, and 10-year), and PFS rates were 89.2% (3-year) and 81.1% (5-year and 10-year). Common toxicities noted in the adjuvant IMRT and CCRT groups were chronic hematology with 9% Grade 3/4 toxicities and acute neutropenia with 19% Grade 3/4 toxicities, respectively. Other toxicities were less than 5%.

Conclusions: For patients with cervical cancer who had undergone radical hysterectomy, IMRT had long-term favorable outcomes compared with the traditional methods of radiotherapy; it also had a low morbidity in early-stage patients with pathological risk factors.

Szu-Wei Huang 黃偲婋
(Y4)

Clinical and pathological characteristics of endometrial cancer patients with loss of mismatch repair expression in Southern Taiwan

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OBJECTIVE: Some cases of endometrial cancer are associated with an aberration in the mismatch repair (MMR) gene. However, limited information was available in Taiwan about this genetic-related disorder. Hence, in this study we attempted to evaluate the prevalence of MMR gene defect and its association with clinico-pathological features in endometrial cancer patients.

MATERIAL & METHOD: Patients who were diagnosed with endometrial cancer between Jan. 2018 and Sep. 2019 were identified. The clinical and pathological data were extracted from medical records. Immunohistochemical (IHC) staining of endometrial cancer tissues for expression of MLH1, PMS2, MSH2 and MSH6 was performed from formalin fixed paraffin-embedded blocks. Prevalence of MMR gene defect and its association with clinico-pathological features were analyzed.

RESULTS: Overall, 130 cases were enrolled in this study and the prevalence of MMR defect was 22.3%. The prevalence rates of MMR defect in different age groups were 8.3% (1/12) in age less than 40, 10% (2/20) in 40 to 50-year age group, 39.1% (18/46) in 50 to 60-year age group and 15.4% (8/52) in age over 60. MMR defect was found more in grade 2/3 tumors (28.2% vs. 13.8%, p=0.049). Nulliparous women with endometrial cancer tend to have lower prevalence of MMR defect (7.7% vs. 27.2%, p=0.036). There was no significant difference of BMI, FIGO stage, histology type, depth of myometrial invasion, lymphovascular invasion, nodal metastasis, and estrogen/progesterone receptor status between the MMR defect and proficient population. There was also no significant difference of prevalence rates between those with and without family history of colon, breast or gynecologic malignancy and synchronous ovarian cancer.

CONCLUSIONS: In our study, 22.3% of endometrial cancer patients had MMR defect. MMR defect was found more in grade 2/3 tumor but less in nulliparous patients. Comprehensive analysis MMR defect in a large patient series will be required to determine the truly overall prevalence rate and its association with clinic-pathological features in Taiwan.

Ching-Yu Cheng **鄭晴予**
(Y5)

Chemotherapeutic Regimens and Chemotherapy-Free Intervals Influence the Survival of Patients with Recurrent Advanced Epithelial Ovarian Carcinoma

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Background: To evaluate factors influencing the outcomes of patients with platinum-sensitive recurrent epithelial ovarian carcinoma (EOC).

Methods: Patients with advanced stage EOC, who received debulking surgery and adjuvant chemotherapy for recurrence, were obtained from the National Health Insurance Research database of Taiwan between 2000 and 2013.

Results: A total of 1038 patients with recurrent advanced stage EOC were recruited. The platinum+ paclitaxel (PT) group had the best 5-year SR (survival after recurrence) compared with the other three groups ($p<0.001$). The hazard ratios (HRs) of 5-year SR for the platinum + liposomal doxorubicin (PD), topotecan (TOP), and pegylated liposomal doxorubicin (PLD) groups were 1.21 ($p=0.07$), 1.35 ($p=0.016$), and 1.80 ($p<0.001$), respectively, compared with the PT group. The PT group also had lower hazard ratios of 5-year SR for patients with chemotherapy-free intervals (CFIs) between 6 and 12 months compared with the other three groups ($p<0.0001$). However, the HRs of 5-year SR did not differ between the PT and PD groups in patients with CFIs > 12 months. Patients with CFIs > 12 months had lower HRs of 5-year SR compared to those with CFIs of 6–12 months, regardless of whether they were treated with platinum-based ($p=0.001$) or non-platinum-based ($p=0.003$) regimens.

Conclusions: Chemotherapeutic regimens and CFIs influenced the outcomes of patients with recurrent EOC. Platinum plus paclitaxel is the best regimen for patients with recurrent EOC with CFIs between 6 and 12 months.

Lan-Yin Huang 黃蘭茵
(Y6)

ER and PR expression in advanced endometrial carcinoma: a cohort study

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Objective: The purpose of this study was to investigate the relationship between tumor hormone receptor expression and the prognosis of advanced endometrial carcinoma.

Materials and Methods: We conducted a retrospective cohort study in a single tertiary medical center by searching the database from National Cheng Kung University hospital, Cancer Center for patients registered as endometrial carcinoma during January 1st 2010 to December 31th 2014. Total 59 patients at advanced stage (stage III and IV) were enrolled.

Immunohistochemistry for ER-alpha and PR-A was performed on tissue specimens. The ER and PR expression were scored in a continuous fashion as the percentage of positive cells ranging from 0% to 100%, and then were dichotomized using a cut point of 1%. We defined marker-positive status as expression at or above 1% and marker-negative meant expression below 1% (≥1% vs. <1%).

We use Cox regression model to evaluate the association between ER and PR expression and patient outcomes (disease-free and overall survival).

Results: In univariate analysis, age at diagnosis, cancer stage, histology type, ER status, and PR status were significantly associated with overall survival. These five variables were included in the multivariate Cox regression, and of these variables, positive PR status were significantly associated with favorable overall survival (HR=0.22, 95% CI 0.06-0.80, p=0.021) independent to age, stage, and histology, but ER status achieved significance (HR=1.32, 95% CI 0.39-4.40, p=0.657).

About disease free survival, cancer stage, histology type, and PR status showed significant association. In multivariate analysis, positive PR expression was significantly associated with favorable disease-free survival (HR=0.12, 95% CI 0.03-0.46, p=0.002) independent of other factors. ER expression wasn’ t associated with disease free survival in univariate analysis, so was not included in the multivariate analysis.

Conclusions: ER expression is not significantly associated prognosis, while PR expression is significantly related to prognosis in advanced endometrial cancer. Positive PR expression is associated with favorable overall survival and favorable disease-free survival.

You-Chen Wang **王佑辰**
(Y7)

BRCA1/2 mutation status in patients with metachronous breast and ovarian malignancies: clues towards the implementation of genetic counseling

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Objective: The characteristics of patients with metachronous breast and ovarian malignancies and the pathogenic role of BRCA1/2 mutations remain poorly understood. We investigated these issues through a review of hospital records and nationwide Taiwanese registry data, followed by BRCA1/2 mutation analysis in hospital-based cases.

Methods: We retrospectively retrieved consecutive clinical records of Taiwanese patients who presented with these malignancies to our hospital between 2001 and 2017. We also collected information from the Data Science Center of the Taiwan Cancer Registry between 2007 and 2015. Next-generation sequencing and multiplex ligation-dependent probe amplification were used to identify BRCA1/2 mutations and large genomic rearrangements, respectively. When BRCA1/2 mutations were identified in index cases, pedigrees were reconstructed and genetic testing was offered to family members.

Results: A total of 12,769 patients with breast cancer and 1,537 with ovarian cancer were retrieved from our hospital records. Of them, 28 had metachronous breast and ovarian malignancies. We also identified 113 cases from the TCR dataset. Eighteen hospital-based cases underwent BRCA1/2 sequencing and germline pathogenic mutations were detected in seven patients (38.9%, five in BRCA1 and two in BRCA2). All BRCA1/2 mutation carriers had ovarian high-grade serous carcinomas. Of the 12 patients who were alive at the time of analysis, five were BRCA1/2 mutation carriers. All of them had family members with BRCA1/2-associated malignancies.

Conclusions: Our results provide pilot evidence that BRCA1/2 mutations are common in Taiwanese patients with metachronous breast and ovarian malignancies, supporting the clinical utility of genetic counseling.

Pei-Chi Wu 吳珮琪
(Y8)

Two-port laparoscopic myomectomy using conventional laparoscopic instruments and glove-port technique: A comparison between an experienced surgeon and trainees

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Purpose: To evaluate the surgical outcome of two-port laparoscopic myomectomy (LM) using conventional laparoscopic instruments and a glove port system.

Methods: A total of 204 women who underwent two-port LM, a modified method to performed LM, between January 2015 and September 2019 in a tertiary center were included in this study. Among them, twenty-one surgeries were performed by 3 trainees (young doctors) under well-supervised by an experienced surgeon. The Fisher exact tests and Mann-Whitney U tests were applied appropriately. A p-value of less than 0.05 was considered statistically significant.

Results: The age and body mass index of the participants were 39.3±6.4 years old and 22.6±3.3 kg/m2. The mean diameter of the largest myomata and the mean number of myomata were 8.5±2.2 cm and 1.7±1.1. Thirty-two (16%) operations removed more than 2 myomata larger than 5cm in diameter. The mean weight of myomata was 281.1±183.1 gm. The operation time was 97.6±40.2 minutes, and the intraoperative blood loss was 99.3±115.2 mL. There were 2 (1%) cases of excessive blood loss (more than 500mL), and 2 (1%) postoperative hematoma. The myoma number, myoma diameter, myoma weight, and intraoperative blood loss were not statistically different between the experienced surgeon and trainees. The only difference was the operation time (92.3±32.2 min vs. 141.2±54 min, $p<0.001$). Two of the operations were converted to 3-port LM due to severe adhesion; meanwhile, none of the surgeries were converted to laparotomy. No patient experienced any major complications, including bowel, ureter, bladder injuries, or incisional hernia. Two patients had post-operative hematoma, and the hematoma resolved shortly after conservative treatment.

Conclusions: Two-port LM is an easy-learning, approachable, safe and efficient surgical method of minimally invasive management for uterine myoma.

Ci Huang **黃琦**
(Y9)

Assessing Adequency of Cervical Specimen and the Clinical Outcomes after Laparo-endoscopy Single-site Cervical Ligament Hysterectomy

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Background: Total hysterectomy would transect ligaments or fascia aroun the cervix, including pubocervical fascia, the transverse cervical ligament (cardinal), and uterosacral ligament (suspend the rectovaginal septum). The subtotal hysterectomy preserves the cervix and cervical ligaments, but patients may worry about cervical neoplasia or cyclical vaginal discharge. The residual endometrial gland in the cervix may cause 5%–20% of women to exhibit cyclic bleeding afterward. To improve the disadvantages mentioned above, we performed laparoendoscopic single-site cervical ligaments sparing hysterectomy (LESS-CLSH)-- laparoscopically conization of the internal orifice of cervix after supracervical hysterectomy and transvaginal external os conization. To access the adequacy of cerical specimen and the clinical outcomes after LESS-CLSH a retrospective cohort study was launched.

MEASUREMENTS AND MAIN RESULTS: A retrospective cohort study. We enrolled fifty-nine women who underwent LESS-CLSH from January 2014 to December 2018 at Hualien Tzu Chi Medical Center. Mean patient age was 46 years, and median (range) parity was 2 (0-5). Four patients (6.7%) were postmenopausal. In most patients (69.4%) adenomyosis with dysmenorrhea was the indication for hysterectomy, and 1 patient (1.6%) had carcinoma in situ (Table 1). The most common cervical pathologic diagnosis was cervicitis (45.7%) (Table 2). Review all the cervical specimens of CLSH patients by senior pathologist. Histopathologic presence of the sqaumocolumnar junction (S-C junction) was present in all cervical specimens. In the following pap smear, the first year found normal limit in 18 patients (32 .1%) and 7 patients (12.5%) at second year (Table 3). The only one CIS patient had also normal limit at the following year. The following clinical outcome of cervicitis and vaginitis found in 18 patients (32%) at first year. No further complication developed in the following year.

CONCLUSION: LESS-CLSH is a new minimally invasive approach of hysterectomy which remove adequate endocervical canal and exocervix because squamous columnar junction can be found in all the cervical specimens. No vaginal bleeding cervical dysplasia or cervical neoplasm were reported after two years follow. The cervicitis and vaginitis could be treat with oral medications without further treatment.