Yi-Chieh Chen 陳怡潔 (Y1)



Bilateral Ovarian Thecomas With Sclerosing Peritonitis Mimicking Epithelial Ovarian Cancer

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Abstract

A rare bilateral ovarian thecomas with sclerosing peritonitis is reported in clinical and pathologic features. Ovarian thecomas are benign ovarian sex-cord stromal tumors that only represented for 0.5-1% of all ovarian tumors. Bilateral ovarian thecomas with sclerosing peritonitis is even more rare condition that less than a hundred case reports were published worldwide.

The patient had small bowel obstruction and persistent massive ascites after total abdominal hysterectomy and bilateral salpingo-oophorectomy. Thus, GnRH agonist and tamoxifen were given. When benign ovarian theomas combining with sclerosing peritonitis, the disease may become life-threatening and multimodality treatment with both surgical and medical treatment remained the most effective treatment to reduce morbidity and even mortality.

Chia-Hao Liu 劉家豪 (Y2)



Synergistic therapeutic effect of low-dose bevacizumab with cisplatin-based chemotherapy for advanced or recurrent cervical cancer

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Background: Cisplatin-based chemotherapy (CBC) is highly efficacious for advanced cervical cancer; its efficacy can be enhanced by combining with 15 mg/kg (standard dose) bevacizumab (BEV). However, this standard dose is associated with various adverse events (AEs). Therefore, in this retrospective study, we analyzed the survival outcomes and AEs in patients with advanced or recurrent cervical cancer treated with CBC in combination with BEV 7.5mg/kg.

Methods: Registered patient data were retrieved between October 2014 and September 2019, and 64 patients with advanced or recurrent cervical cancer treated with CBC + BEV (n = 21) or CBC alone (n = 43) were analyzed. The primary endpoints were progression-free survival (PFS) and overall survival (OS); the secondary endpoints were the frequency and severity of AEs. The Cox proportional-hazards model was applied to explore prognostic factors associated with PFS and OS.

Results: The 1-, 2-, and 3-year PFS rates (95% CI) were 36.24% (22.0-50.5), 20.7% (9.8-34.2), and 17.7% (7.7-31.1) for the CBC group; and 71.4% (47.1-86.0), 51.0% (27.9-70.1), and 51.0% (27.9-70.1) for the CBC + BEV group, respectively. The 1-, 2-, and 3-year OS rates were 62.6% (46.4-75.18), 32.4% (18.8-46.9), and 23.2% (11.2-37.6) for the CBC group; and 85.7% (61.9-95.1), 66.6% (42.5-82.5), and 55.5% (27.1-76.7) for the CBC + BEV group, respectively. The CBC + BEV group presented higher PFS and OS rates, p = 0.003 and p = 0.005, respectively. Proteinuria (6 vs 9, p = 0.025) and hypertension (0 vs 10, p < 0.001) were less common, but anemia was more common in the CBC group (35 vs 11, p = 0.021).

Conclusion: Overall, CBC + BEV significantly improved the PFS and OS compared with CBC alone. CBC + BEV also prevents severe AEs and hence is an efficacious and safe therapeutic option.

Yi-Liang Lee **李易**良 (Y3)



The Potential Role of Cell Membrane and Transporter related Functionomes for Tumorigenesis inferred by the Gene Ontology-Based Integrative Analysis of Ovarian Clear Cell Carcinoma

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Background: Epithelial ovarian cancers (EOCs) are fatal and obstinate among gynecological malignancies in advanced stage or relapsed status, with serous carcinomas accounting for the vast majority. Ovarian clear cell carcinoma (OCCC) is the second most common epithelial ovarian carcinoma (EOC). It is refractory to chemotherapy with a worse prognosis after the preliminary optimal debulking operation, such that the treatment of OCCC remains a challenge. According to the result of our previous finding of immunofunctionomes analysis in OCCC, we arrange a further comprehensive integrated analysis of functionomes for early and advanced stages of OCCC.

Method: DNA microarray gene expression profiles were used to convert 85 OCCCs and 136 normal controls into the gene ontology (GO) based functionomes. We utilized the functionome-based speculative model from the aggregated obtainable datasets to explore the expression profiling data among the early and advanced stages of OCCC by analyzing the functional regularity patterns and clustering the separate gene sets. Quantified biological functions defined by 14998 GO terms downloaded from the Gene Expression Omnibus (GEO) database were used.

Results: The results exhibited the top 5 common dysregulated biomolecular functions that could be categorized as the cell membrane and transporter related group and 3 meaningful related Differentially Expressed Genes(DEGs) including ATP1A2, P2RX4 and SLC9A3R1 were sorted out. We also discovered and select interactively 16 GO-based dysregulated pathogenic pathways that could be reclassified as 4 functional genetic groups (MAN, EDEM, CYP, and SLC series).

Conclusion: The result of these important findings demonstrated the dysregulated functionomes and dysfunctional pathways as potential roles during the tumorigenesis of OCCC and may be helpful for the diagnosis and therapy in the future.

Yen-Han Wang **王彥**涵 (Y4)



DOCK4 could be a Potential Biomarker for the Outcome of Epithelial Ovarian Cancer

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Purpose: To investigate the expression of *DOCK4* and the correlation with the clinical outcomes in epithelial ovarian cancer patients.

Materials and Methods: The gene expression of *DOCK4* were evaluated by quantitative real-time PCR in 198 epithelial ovarian cancer patients. The correlation of *DOCK4* expression with the clinical outcomes were analyzed.

Results: The mean expression level of *DOCK4* was higher in the advanced staged $(0.00766 \pm 0.001540 \text{ versus } 0.00318 \pm 0.000689, p=0.009)$, and recurrent $(0.00827 \pm 0.001762 \text{ versus } 0.00372 \pm 0.001206, p=0.034)$ patients. Advanced stage (H.R.: 2.59, 95% C.I.: 1.39-4.86, P=0.003), optimal debulking (H.R.: 0.47, 95% C.I.: 0.33-0.67, P<0.001) and high *DOCK4* expression (H.R.: 1.89, 95% C.I.: 1.30-2.75, P=0.001) were independent factors for disease recurrence. Advanced stage (H.R.: 13.46, 95% C.I.: 2.60-69.61, P=0.002), optimal debulking (H.R.: 0.27, 95% C.I.: 0.16-0.45, P<0.001) and high *DOCK4* expression (H.R.: 2.38, 95% C.I.: 1.46-3.89, P<0.001) were independent factors for disease death.

Conclusions: high *DOCK4* expression may correlate with disease recurrence and death in epithelial ovarian cancer patients and could be a potential prognostic biomarker.

Ting-Fang Lu 呂亭芳 (Y5)



Laparoscopy Compared with Laparotomy for Comprehensive Surgical staging for clinical stage 1 endometrial cancer: a single institute experience in Taiwan

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Objective: Endometrial cancer is the most common gynecological cancer in developed countries and accounts for 6% of all cancers in women. In Taiwan, lifestyle-related changes in the recent decades have led to a rise in the incidence of obesity and metabolic syndrome-related diseases, which are potential risk factors for endometrial cancer. With the recent advances in laparoscopic equipment and knowledge, laparoscopic surgery is widely accepted as safe and feasible for managing benign gynecologic disease, and several authors have reported laparoscopic approaches for the treatment of endometrial cancer. As many gynecologists are moving toward laparoscopy, this study will examine the outcome of both surgical methods.

Materials and Methods: We retrospective reviewed 689 patients with clinical stage 1 endometrial cancer from 2010 to 2020 in our institute. All patients underwent comprehensive surgical staging procedures including total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy and some patients also received paraaortic lymphadenectomy. The safety, morbidity, progress free survival and overall survival rates of the two groups were compared.

Results: 417 patients received laparoscopic surgery and 272 underwent laparotomy. Operation time for the laparoscopic procedure was 244(204-284) minutes, which showed significant difference from the 265(230-300) minutes (p<0.001) of the laparotomy group. The estimated blood loss of patients undergoing laparoscopic surgery was 75(50-100) mL. This was significantly less than that of the laparotomy group 430(250-650 mL, p<0.001). The laparoscopic group had an average of 19 nodes retrieved, as compared to 20 pelvic nodes retrieved in the laparotomy group. The mean hospitalization duration was significantly longer in the laparotomy group than the laparoscopic group (9 and 4 days, p=0.001). The laparoscopic group has statistically significant difference in the 5 year overall survival rate(98.5% and 88.8%, P<0.001) and progress free survival (93.2% and 83.0%, P<0.001). More adverse risk factors including grade 3, not endometrioid type, lymph node metastasis were also found in laparotomy group.

Conclusion: Laparoscopic operation was an effective surgery for clinical stage 1 endometrial carcinoma in clinical setting. Compared to laparotomy staging, laparoscopic staging has good survival rate with less hospital stay and complications.

Jung Chen 陳瑢 (Y6)



Outcome and Optimal Therapy of Uterine Serous and Clear Cell Carcinomas: a Population-based Study

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Objective: Uterine serous carcinoma (USC) and uterine clear cell carcinoma (UCCC) have been considered of having aggressive tumor biology and poor outcomes compared to endometrioid-type uterine cancer. The purpose of this study is to identify the optimal adjuvant treatment strategies relevant to prolong overall survival (OS) in the rare gynecologic cancers of USC and UCCC.

Material and methods: The Taiwan Cancer Registry Long-Form Database was queried from 2009 to 2018 for uterine serous carcinoma (USC) and uterine clear cell carcinoma (UCCC) patients who underwent primary surgery with or without the other adjuvant therapies as definitive treatment. Overall survival was calculated using the Kaplan-Meier analysis and log-rank test was used to compare between groups.

Results: A total of 976 patients with USC or UCCC histology type were eligible for analysis. For patients with USC (n = 638), the five-year OS was 85.4% for stage I, 79.7% for stage II, 40.2% for stage III, and 23.3% for stage IV. For patients with UCCC (n = 338), the five-year OS was 88.1% for stage I, 74.1% for stage II, 65.1% for stage III, 22.8% for stage IV. No difference was observed on the five-year OS after receiving different adjuvant treatments in early-stage (FIGO I/II) USC patients (p=0.54) and in early-stage UCCC patients (p=0.45). Combined adjuvant therapy with chemotherapy and radiation had the best five-year OS with 41.6% for stage III and 44.8% for stage IV USC patients compared with the other adjuvant strategies (p=0.0015). Combined adjuvant therapy also showed the best five-year OS (72.6%) for advanced stages (III/IV) UCCC patients (p=0.0005, log rank test).

Conclusions: Early-stage USC and UCCC had similar survival regardless of which adjuvant therapy. For advanced-stage USC and UCCC, combined adjuvant therapy with chemotherapy and radiation could improve survival after comprehensive staging surgery.

Kai-Yuan Jheng 鄭凱元 (Y7)



Risk of head-and-neck cancer following a diagnosis of moderate cervical intraepithelial neoplasia: analyses from national health insurance research database in Taiwan

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Intruduction: More than 99% of cervical carcinomas was associated with Human papillomavirus (HPV) infection. High risk HPV type infection was thought as essential for cervical moderate dysplasia and carcinoma. Similar risk was found between HPV infection and head and neck squamous cell carcinomas (HNSCCs). The FDA also approved the HPV vaccine for HNSCCs prevention. Epidemiological studies have shown that patients with history of cervical cancer or CIN3/AIS have a higher risk of HNSCC than women without such a history. Thus, we want to know if the lifetime risk of head and neck cancer in patients with history of moderate cervical dysplasia is higher compare to patients with history with mild dysplasia.

Methods: This study is conducted to explore the data from national health insurance research database in Taiwan (n = 16,644) during a 14-year follow-up period (2001 ~ 2015). We identified patients with diagnosis of cervical dysplasia (ICD9 code = 622.1), which included mild and moderate dysplasia (N=9,385), and excluded patients had history of cancer or diagnosed as cancer within 3 months after index date. We divided them into two groups according to the history of conizaton (procedure code: 80205) within one year after the diagnosis of cervical dysplasia. We then compared the incidence rate of newly diagnosed cases of cervical, vulva and vaginal cancer, as well as cases of head and neck cancer, between those 2 groups

Results: Compared with women with mild cervical dysplasia, women with moderate cervical dysplasia are still at higher risk of developing cervical cancer in the future, even after conization. However, compared with mild dysplasia, the risk of further head and neck cancer in patients with moderate dysplasia is not significant.

Discussion: Squamous cell carcinoma of the head and neck can be classified as keratinized or nonkeratinized type. The former is associated with smoking and alcohol consumption and the later is HPV-involved. Based on our hypothesis, the linkage between cervical moderate dysplasia and head-and-neck cancer is persistent HPV infection. However, our data didn't show a significant increased risk on head and neck cancer in women with a history of CIN2 while comparing with women with only mild dysplasia. The result may caused by the sparse cases of head and neck cancer in our study population, the insufficient following up duration or the low prevalence of persistent HPV infection of oropharynx in Tainwan. However, the spectrum of diseases between cervical cancer, severe dysplasia and mild dysplasia should still be considered.