The third CJUA annual meeting

2009

China-Japan urological association

PROGRAM & ABSTRACTS

Date

April 17, 2009

Venue

OKAYAMA CONVENTION CENTER

14-1 Ekimotomachi, Okayama, Japan

CJUA Home-page URL: http://www.uro.jp/nichu/index.html

PROGRAM of the third CJUA annual meeting

(2009.4.17　Okayama Japan)

14:00 to 14:10　Opening Address

Prof. Hiromi Kumon, President of CJUA (Japan)

14:10 to 14:50　Special Lecture

Chairman: Prof. Hiromi Kumon, Okayama University

Progress and Future of p53 Gene Therapy in China

Prof. Shan-wen Zhang, Peking University School of Oncology

14:50 to 15:50　Session I (8 minutes presentation following 4 minutes discussion)

Chairmen: Atsushi NAGAI, Kawasaki, Japan
Xianghua Zhang, Beijing, China

1. **The overactive bladder symptom score (OABSS) is a useful assessment tool for evaluating treatment-related change in clinical trials with OAB patients as well as the overactive bladder questionnaire (OAB-q).**
   Yoshiyuki Ishiura　NHO Kanazawa Medical Center, Japan
2. **Efficacy and Safety of Tamsulosin in Chinese Patients with Lower Urinary Tract Symptoms Associated with Benign Prostatic Hyperplasia**
   Xianghua Zhang　Peking University First Hospital, China
3. **Efficacy and Safety of Silodosin, a Novel α_{1A}- Adrenoceptor Selective Antagonist for Treatment of Benign Prostatic Hyperplasia**

Ning-chen Li　Silodosin clinical study group, China

4. **Influence of polymorphisms and expression of chromogranin A and endothelin-1 on the development and progression of prostate cancer**
   Zhiyong Ma　Akita University School of Medicine, Japan

5. **SNP genotyping is useful for genetic predisposition for prostate cancer in Japan**
   Peng Huang　Okayama University, Japan

15:50to 16:50　Session II (8 minutes presentation following 4 minutes discussion)

Chairmen: Yoshiyuki Kakehi, Kagawa, Japan
Jianbin Bi, Shenyang, China

6. **Diagnosis and treatment of Renal cell carcinoma associated with von Hippel-Lindau disease**
   Xue Wei　Renji Hospital, Shanghai Jiaotong University Medicine School, China
7. **Ten-year Biochemical Disease-free Survival After High Intensity Focused Ultrasound (HIFU) For Localized Prostate Cancer: A Comparison Of Three Different Generation Devices**
   Toyoaki Uchida　Tokai University Hachioji Hospital, Japan
8. **A new urinary diversion by ileal reservoir with extracorporal self-controllable urination**
   Xiuheng Liu　Renmin Hospital, Wuhan University, China
9. **Honokiol, a natural plant product from magnolia tree, inhibits the bone metastatic growth of human prostate cancer cells**
   Katsumi Shigemura　Kobe University, Japan
10. **Retroperitoneoscopic nephroureterectomy with transurethral bladder-cuff excision for renal pelvic and ureteral tumors.**
    Liu Xiao-qiang　The second hospital of Tianjin medical university, China

16:50 to 17:00　Closing Address

Prof. Yanqun Na, President of CJUA (China)

Special Lecture

Progress and Future of p53 Gene Therapy in China

ZHANG Shan-wen
Peking University School of Oncology

Tumor suppresser gene p53 well known for its structure and function, widely regarded as the genome guardian of cells, plays a key role in cell cycle control, apoptosis, and inhibition of tumor cell proliferation; especially as a transcription factor, in cellular responses to DNA damage including irradiation, hyperthermia, and cytotoxic agents.

Wild-type p53 gene promotes cell cycle arrest and apoptosis of tumor cells after irradiation, but mutated p53 abrogates this response and induces resistance to radiation. Replacement with normal p53 gene using viral vectors results in suppression and reversal of the malignant phenotype. P53 gene transfer induces radiosensitization: a strategy to convert a radio-resistant phenotype into a radio-sensitive one.

Adp53 is an E1 substituted replication-incompetent recombinant adenovirus encoding the human p53 gene.

Recombinant human p53 adenovirus injection (trademarked as Gendicine) was approved to market by the SFDA in October 2003. Although the product is primarity used for nasopharyngeal carcinoma and other head-and-neck cancers, and is off-label used for cervix, pancreas, liver and other cancers at a late-stage, especially for sarcoma which cannot be easily treated by conventional methods. Adp53 is normally injected into solid tumors, although intra-locoregional arterial infusion, and intrathoracic /intraperitoneal infusion are also used. Now p53 gene therapy mostly in combination with radiotherapy, hyperthermia, or chemotherapy. Up to now, more than 3000 patients with cancer have been treated with Adp 53 in china.

Study of Clinical mechanism: Expression of p53 gene and p53 target gene assayed by immunohistochemistry (IHC) in tumor simple taken 48h after intratumoral injection of Adp53. Up-regulation of cell cycle relative gene p21 and apoptosis relative gene Bax and down-regulation of VEGF were observed in postinjection tumor biopsy by using IHC. Adp53-specific p53 mRNA was detected by RT-PCR analyses of tissue samples in 16 (94.1%) of 17 assessable samples taken 48h after intratumoral injection of Adp53.

Clinical Study: Between Oct. 2001 to May. 2003, a randomized controlled clinical trial on Adp53 combined with radiotherapy (GRT group) in 42 patients with nasopharyngeal carcinoma (NPC) was compared with a control group of 40 patients

with NPC treated with radiotherapy alone (RT group). In the GRT group, Adp53 was intratumorally injected once a week for 8 weeks. Concurrent RT (70Gy in 35 fractions) was given to nasopharygeal tumor and neck lymph node. Patients and tumors were monitored for adverse events and response, respectively.

Complete response rate in the GRT group was observed at 2.73 times that of RT group (66.7% vs. 24.4%). Six-year follow-up data showed that Adp53 significantly increased the 5-year locoregional tumor control rate by 25.3% for patients with NPC treated with irradiation (P=0.002). The 5-year overall survival rate and 5-year disease-free survival rate of GRT group were 7.5% (P=0.34) and 11.7% (P=0.21) higher than that of RT group. No dose-limiting toxicity and adverse events appeared, except for transient fever following Adp53 administration.

15 patients with cervix cancer at a late-stage IIB (2 cases) or IIIB (13 cases) treated by Adp 53 in combination with radiation totally got complete response. 5-year survival rate was 85.7% higher than that of radiotherapy alone before.

p53 gene was mutated in 70% of patients with pancreas cancer induces high malignant phenotype, high recurrent rate, and very low 5-year survival rate (only 1 to 3%). So 9 patients with unresectable pancreas cancer (4 primary and 5 metastasis) treated with Adp 53 in combination with radiation got a good response, mean survival time was 13.2 months, that equate to results of surgery for patients with pancreas cancer at a early stage .

Higher incidence rate of p53 gene mutation was significantly correlated to worse survival and successful Adp53 gene transfer synergistically inhibited growth and metastasis in patients with bladder cancer and prostate cancer. A new strategy of Adp53 to increase locoregional control for urology tumors should be suggested.

Relative article was published in JCO, February 2009.

Jian-ji Pan, Shan-wen Zhang*, et al. Effect of Recombinant Adenovirus-p53 Combined With Radiotherapy on Long-Term Prognosis of Advanced Nasopharyngeal Carcinoma. Journal of Clinical Oncology, 2009, 27 (5):799-804. J.P. and S.Z. contributed equally to the article.*Corresponding author: Shan-wen Zhang （IF15.484）Fucheng Rd, Haidian District, Beijing 100036, People’s Republic of China

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ABSTRACTS

1. The overactive bladder symptom score (OABSS) is a useful assessment tool for evaluating treatment-related change in clinical trials with OAB patients as well as the overactive bladder questionnaire (OAB-q).

Yoshiyuki Ishiura Masashi Iijima, Kiyoshi Koshida
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AIMS OF STUDY: Overactive bladder (OAB) is characterized by symptoms of urinary frequency and urgency, and has been shown to have significant impact on health-related quality of life (HRQL). The overactive bladder questionnaire (OAB-q) is a useful tool for measuring OAB-related HRQL in clinical management [1]. The overactive bladder symptom score (OABSS), which integrates four OAB symptoms (daytime frequency, nighttime frequency, urgency and urgency incontinence) into a single score, was developed as a symptoms assessment tool [2]. There was no report that discussed relations of OABSS and OAB-q till now. This study compared the OABSS with the OAB-q and examined the responsiveness of anti-muscarinic treatment. The relations with age, gender, treatment history and presence of urinary incontinence were also examined.

MATERIALS AND METHODS: OAB was diagnosed by more than three points of OABSS with the presence of urgency. OAB patients were treated with anti-muscarinic agent administration for 4 to 12 weeks in our out-patient clinic. The OABSS and the OAB-q were collected at pre- and post-treatment. The relation between the OABSS and the OAB-q and responsiveness of anti-muscarinic treatment were analyzed. The relation between the responsiveness of anti-muscarinic treatment for OAB-related symptoms and HRQL disorders and the other factors such as age, gender, treatment history, presence of urinary incontinence were examined.

RESULTS: A total of 46 patients enrolled (mean age = 72.7 years, 56.5% male, 73.9% OAB wet). The average point of sum score of the OABSS, daytime frequency, nighttime frequency, urgency, and urgency incontinence before therapy was 8.3, 0.9, 2.1, 3.3, and 2.1 respectively. In a point of OAB-q subscale before therapy, the average of symptoms bother, coping, concern, sleep, social interaction, and HRQL total was 29.1, 67.2, 75.4, 73.0, 82.8, and 73.8 respectively. Before therapy, the sum score of the OABSS was significantly correlated with all OAB-q subscales except for social interaction. Correlation with OAB-q at pre-treatment was examined, which was greatest for the sum score of the OABSS, followed by urgency, nighttime frequency, urgency incontinence, and daytime frequency. The significant correlation was seen between age and the OABSS, but not seen between age and the OAB-q.

The sum score of the OABSS was significantly decreased (6.0) after therapy. Daytime frequency (0.7), nighttime frequency (1.6), urgency (2.3), and urgency incontinence (1.4) were also significantly decreased. After treatment, significant improvements occurred in all OAB-q subscales. The average of symptoms bother, coping, concern, sleep, social interaction and HRQL total was 24.7, 74.3, 82.0, 76.9, 88.9 and 82.3 respectively. The correlation was not recognized in age and degree of the responsiveness of anti-muscarinic treatment for OAB-related symptoms and HRQL. The differences of the responsiveness of anti-muscarinic treatment by the gender and presence of urinary incontinence were not seen, too. OAB patients without treatment history were significantly improved by anti-mucarinic treatment rather than OAB patients with treatment history. As for the cases that sum score of the OABSS improved more than two points after treatment, each subscale of the OAB-q were improved by predominance. On the contrary, in the cases that improvement was not seen in sum score of the OABSS after treatment, all subscales of the OAB-q were not improved.

CONCLUDING MESSAGE: The OABSS had a significant correlation with individual OAB-q subscales. Anti-muscarinic treatment had improved both OABSS and OAB-q.

OAB symptoms have correlation with OAB-related HRQL and symptom bother. Both OAB-related symptoms and HRQL were improved by anti-muscarinic drug administration. The OABSS appears to be a useful outcome measure for evaluating treatment-related symptoms change in clinical trials and practice with OAB patients as well as the OAB-q.

2. Efficacy and Safety of Tamsulosin in Chinese Patients with Lower Urinary Tract Symptoms Associated with Benign Prostatic Hyperplasia

Xianghua Zhang

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OBJECTIVE: To review and evaluate the efficacy and safety profile of tamsulosin in the treatment of Chinese patients with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH).

DATA SOURCES: A systematic literature search of MEDLINE, China National Knowledge Infrastructure (CNKI) and Wanfang Database for both English and Chinese studies about the efficacy and safety profile of tamsulosin in the treatment of Chinese patients with LUTS/BPH through December 2008 (including an Literature

to be published soon).

RESULTS: Seven studies (1 for English and 6 for Chinese) were involved, these studies not only investigated the short-term and long-term efficacy and safety profile of tamsulosin in the treatment of Chinese patients with LUTS/BPH, but also including certain special patients such as patients concomitant hypertension and sexual dysfunction. The efficacy of tamsulosin on patients with different prostate volumes was also investigated in one study. Tamsulosin may rapidly relieve symptoms, improve quality of life (QOL) and urodynamics parameters of Chinese LUST/BPH patients with all different prostate volume, and the efficacy sustained in long-term; it also may improve sexual function of BPH patient. Tamsulosin demonstrates good safety profile in long-term, with lower incidence of overall adverse events and almost no effect on blood pressure, could be effectively and safely used in patients with BPH and concomitant hypertension. In two clinical controlled trials, tamsulosin demonstrates better efficacy compared with finasteride and terazosin, and the incidence of adverse events for tamsulosin is obviously lower than terazosin.

CONCLUSIONS: Tamsulosin monotherapy has a favorable efficacy and safety profile in Chinese patients with LUTS/BPH and can be used as the initial treatment option.

3. Efficacy and Safety of Silodosin, a Novel α_{1A}- Adrenoceptor Selective Antagonist for Treatment of Benign Prostatic Hyperplasia

Ning-chen Li* Qiang Ding, Wei Zhang, Song-liang Cai, Shi-ping Chen, Yi-ran Huang, Zhang-qun Ye, Chui-ze Kong, Yan-qun Na, Silodosin clinical study group, China

OBJECTIVE: To study the efficacy and safety of a selective α_{1A}-adrenoceptor antagonist silodosin for treatment of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH).

METHODS: This is a randomized, double-blind, placebo-controlled clinical studies on silodosin. The eligible subjects with LUTS caused by BPH were assigned randomly into silodosin group or placebo group at ratio of 2:1, receiving either 4mg bid silodosin (8mg/day) or placebo for 12 weeks. Subjects were evaluated in 2, 4, 8 and 12 weeks of treatment. The change in the total score of the international prostate symptom score (I-PSS) was used to assess the efficacy after 12 weeks of treatment. The change of maximum urinary flow rate (Q_{max}), quality of life (QOL) score, the change of total I-PSS score after 1 week and 2 weeks treatment were also observed.

All adverse events during the treatment period were recorded and assessed for severity and causal relationship with taking the investigational products.

RESULTS: Totally 516 subjects were enrolled into two groups, 344 to silodosin group and 172 to placebo group. Full analysis set (FAS), comprised 501 subjects, with 338 in silodosin group and 163 in placebo group. There were no significant differences among the two groups in baseline characteristics. The results showed that, compared with the placebo group, the decrease of total I-PSS in silodosin group was significant after 12 weeks of treatment (p=0.0099), and the least square mean between silodosin group and the placebo group was –1.45 (95% confidence interval:–2.55;-0.35). The total I-PSS were significantly greater decreases with silodosin than placebo from 1 week (p=0.0007) and 2 weeks (p=0.0002) after starting treatment. The QOL score changes for silodosin group and placebo group were –1.74±1.37 and –1.40±1.31 respectively, showing statistical difference (p=0.0073). Of the total 511 subjects evaluated for safety profile, 123 subjects reported adverse events in the silodosin group and 39 subjects in the placebo group and the incidence rate were 35.9% and 23.2% respectively. The incidence rates of drug-related adverse events were 30.0% in silodosin group and 19.1% in the placebo group. The most common drug-related adverse events in silodosin group were abnormal ejaculation (7.6%), dry mouth (4.4%), dizziness (3.5%) and in the placebo group were dizziness (4.2%), rash (3.0%), and dry mouth (2.4%).

CONCLUSIONS: Selective α_{1A}- adrenoceptor antagonist silodosin could remarkably improve the symptoms and life quality of patients with BPH. The high efficacy and safety of silodosin in treatment for BPH patients with LUTS were confirmed in this Chinese population.

4. Influence of polymorphisms and expression of chromogranin A and endothelin-1 on the development and progression of prostate cancer

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INTRODUCTION AND OBJECTIVE: Neuroendocrine markers, chromogranin A (CgA) and endothelin-1 (ET-1), are found to be overexpressed in prostate cancer patients. Recently, it has been reported that CgA triggers ET-1 release, in a

dose-dependent manner, in human vein endothelial cells. This study investigates the influence of polymorphisms and expression of CgA and ET-1 on the development and progression of prostate cancer.

METHODS: The genetic polymorphism study was conducted on 435 prostate cancer patients, 133 benign prostatic hyperplasia (BPH) patients and 115 were controls. DNA sequencing and restriction fragment length polymorphism (RFLP) analysis were used to check the seven polymorphisms (−1106 to −57) in the promoter region, and the Glu264Asp polymorphism in the exon 6 region of the CgA. Haploview software, version 3.32 (Daly Lab, MIT, Cambridge, MA) was used to evaluate the linkage disequilibrium status. Expression of CgA and ET-1 was studied using immunohistochemical (IHC) analysis of prostate cancer specimens obtained from 114 stage A–D1 prostate cancer patients who underwent radical retropubic prostatectomy, and from 27 bladder cancer patients, as normal controls, who underwent radical cystectomy.

RESULTS: Since strong linkage disequilibrium was observed among the seven polymorphisms in the promoter region of CgA, only −415T/C polymorphism was analyzed. The −415T/C polymorphism showed no relationship with the development, progression, and prognosis of prostate cancer, or with the IHC grade of CgA and ET-1. The Glu264Asp polymorphism of CgA showed a dominant effect on the development of prostate cancer. Compared to the CC genotype, the GC and GG genotypes conferred 2.148 and 2.390 times higher risk of prostate cancer, respectively. However, the Glu264Asp polymorphism showed no relationship with Gleason score, progression and prognosis of prostate cancer, and CgA or ET-1 IHC grade. BPH region in the prostate cancer specimens showed higher CgA and ET-1 IHC grade than that in the control specimens ($p = 0.033$, $p = 0.006$). The CgA IHC grade was found to be associated with the clinical stage ($p = 0.005$) and prostate-specific antigen (PSA) failure ($p = 0.016$) after radical prostatectomy. ET-1 IHC grade was found to be associated with the Gleason score ($p = 0.007$).

CONCLUSIONS: The Glu264Asp polymorphism of CgA was found to be associated with the development of prostate cancer. IHC grade of CgA and ET-1 were observed to be associated with the clinical stage and Gleason score, respectively. Furthermore, IHC grade of CgA was found to be associated with PSA failure, after radical prostatectomy. Thus, CgA and ET-1 may play an important role in the development and progression of prostate cancer.

5. SNP genotyping is useful for genetic predisposition for prostate cancer in Japan

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We have genotyped more than 50 non-synonymous Missense-SNP of cancer-related genes in 162 prostate cancer patients and 135 matched healthy males in Japan. Twelve SNP of 10 genes were significantly affected the incidence of prostate cancer. These genes included 2 DNA-repair genes, 5 tumor suppressor genes, and 1 each of metabolizing enzyme gene, chromosome-segregation gene and apoptosis regulator gene. Cancer-associations of these 9 of 12 SNP are novel findings. Eleven associations included 9 high-risk and 2 protective associations, odds ratios (OR) of which ranged between 0.42 – 12.2, and an average statistic power by the Cochran-Armitage formula was 96% and 88% at the 0.05 and 0.01 significance level, respectively.

Thus, our novel way of combining the risk factors of the statistically significant SNP genotypes would be useful for clinical application to predict prostate cancer predisposition of males in Japan and may contribute for prevention and early detection of the disease. This strategy can be applied for other malignancies and for other ethnic populations by choosing proper SNP combinations.

Furthermore, in 2008's competition for government Special Coordination Funds for Promoting Science and Technology, Okayama University's proposal of "An Asia-wide translational research on high-risk group detection based on ms-SNP and IL-12 immunogene therapy for prostate cancer" has been adopted to consolidate translational research infrastructure in Asia with the cooperation of top institutes in China, Korea and Singapore.

6. **Diagnosis and treatment of Renal cell carcinoma associated with von Hippel-Lindau disease**

Zhang Jin, Xue Wei Liu Dong-ming, Huang Yi-ran, Zhou Li-xin, Chen Hai-ge, Chen Qi

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OBJECTIVE: To present our experience about the management of RCC associated with von Hippel-Lindau (VHL) disease.

METHODS: Clinical data were analyzed retrospectively from 28 cases (16 males and 12 females) with RCC associated with VHL disease, of whom 15 had bilateral RCC and 13 had unilateral RCC. VHL germline mutation was analyzed in 25 cases. Nephron sparing surgery (NSS) or Radical nephrectomy was performed in 24 cases.
RESULTS: VHL germline mutations were detected in 25 cases including 14 asymptomatic cases. Among 29 solid renal tumors in 9cases observed for a mean time of 43.6months (range 12 to 86 months), the median increase in tumor size was 0.531cm/ year. There were 19(65.5%) tumors >3cm at the end of follow-up but only one developed retroperitoneum lymph nodes metastasis. A total of 87 solid tumors were removed and 62 (71.2%) solid tumors were managed by NSS. Pathological results showed 86 clear cell carcinomas (73 Fuhrman I and 12 Fuhrman II) and 1 calcified lesion. During mean follow-up of 49.5 months, local recurrence occurred in 4 cases treated with NSS; 26 patients were alive at the end of follow-up.
CONCLUSIONS: DNA testing is helpful in the earlier detection of asymptomatic patients. Most solid renal tumors in VHL disease grow slowly. Many of the tumors > 3 cm may still be indolent and do not metastasize during longer follow-up and can be observed. NSS is effective and safe for RCCs in VHL disease.
KEYWORDS: Hippel–Lindau disease, germline mutation, renal cell carcinoma, nephron -sparing surgery, natural history.

7. **Ten-year Biochemical Disease-free Survival After High Intensity Focused Ultrasound (HIFU) For Localized Prostate Cancer: A Comparison Of Three Different Generation Devices**

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INTRODUCTION: HIFU is recognized as a minimally invasive treatment option for localized prostate cancer. The purpose of the study was to assess the long-term outcome of HIFU for prostate cancer.
METHODS: From January 1999, a total of 662 patients who received HIFU with at least a 1-year follow-up were treated with three different types of Sonablate® (Focus surgery, Indianapolis, USA) devices. Thirty-two patients were treated with Sonablate® 200 (S200) from 1999 to 2001, 406 patients with Sonablate® 500 (S500) from 2001 to 2005 and 224 patients with Sonablate® 500 version 4 (V4) from 2005-2008. Biochemical failure was defined according to the criteria recommended

by the revised American Society for Therapeutic Radiology and Oncology (ASTRO), i.e., a rise of 2 ng/ml or more above the nadir PSA, consensus panel. None of the patients received a post-HIFU androgen deprivation or other anticancer therapy before the documentation of a biochemical failure. The Kaplan-Meier analysis and log-rank test were employed for the analysis.

RESULTS: The mean age, PSA and Gleason score in S200, S500, and V4 groups were 71, 68, and 67 years, 15.4, 12.3, and 10.2 ng/ml, and 5.6, 6.3, and 6.6, respectively. The mean operation time in S200, S500, and V4 groups were 174 min, 123 min, and 68 min, respectively. The mean operation time was shortened in V4 group ($p<0.0001$). The mean follow-up months in S200, S500, and V4 groups were 46, 34, and 21 months, respectively. The biochemical disease-free survival rate (BDFR) in all patients was 57% in 8 years. The BDFR in 8 years in patients with S200 and S500 groups were 56% and 53%, and BDFR in 3 years in patients with V4 group was 83%. The BDFR in the low, intermediate, and high risk groups were 100%, 53%, and 30% in S200, 69%, 48%, and 46% in S500, and 95%, 88%, and 65% in V4 group, respectively. The negative prostate biopsy rate after HIFU was 100% in S200, 79% in S500 and 93% in V4 group. Post operative urethral stricture, epididymitis, and urinary incontinence (grade I) were noted in 20.7%, 5.7%, and 1.5% of the patients, respectively. Erectile dysfunction (IIEF-5 score $\leq$ 7) was observed in 40% in the S500 and in 34% in the V4 group.

CONCLUSIONS: HIFU is indicated as the primary therapy for prostate cancer for with low- and intermediate-risk patients (T1-T2b N0M0 disease, a Gleason score of$\leq$7, a PSA level of<20 ng/mL) and those with a prostate volume of less than 40 mL. The clinical outcome has significantly improved over the years due to technical improvements in the device.

8. A new urinary diversion by ileal reservoir with extracorporal self-controllable urination

Xiuheng Liu Xiaobin Zhang, Fan Cheng

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BACKGROUND: Total cystectomy and urinary diversion are the most effective treatment for patients with invasive bladder cancer, severe bladder contraction, vesicorectal or vesicovaginal fistula and other urological diseases. However, what is the most satisfactory procedure for bladder substitute remains controversial. Various types of urinary diversion including many new continent reservoir have been developed, however no one is good enough to meet the needs of all patients.

Exploring more satisfactory way of urinary diversion is still the key subject of urology.

OBJECTIVE: To investigate the feasibility and effect of the urinary diversion by ileal reservoir with self controllable urination.

METHODS: A segment of 40 cm ileum was taken, from which, the middle 24 cm portion was made into N shaped reservoir, the proximal 6 cm ileum was used as afferent limb. The distal 10cm ileum was pulled out off the stoma where the two skin flaps were taken and encircled the efferent ileum to constitute the urinary outflow. A urinary controller similar to penile clamp was applied to control the urination with a balloon. Postoperative urodynamic examination of the reservoir and X ray photography (KUB+IVU, retrograde) were taken, and body metabolic changes were observed.

RESULTS: The procedure was applied on 32 patients. All the patients recovered well from the operation and were followed up for 3 to 56 months. Biochemical detection of metabolism revealed normal levels of electrolytes, renal function and hepatic function after operation. On first month, the reservoir reached a maximum capacity of (260 ± 60) ml, a full filling pressure of (33.2 ± 9.5) cmH2O, a maximum urinary flow rate of (18.4 ± 5.6) ml/s, and had poor compliance without residual urine. On 48 month, the human reservoir reached a maximum capacity of (380±90) ml, a full filling pressure of (33±5.5) cmH2O, a maximum urinary flow rate of (24.±6.5) ml/s, and had good compliance without residual urine. Postoperative X ray photographical examinations showed good renal function and structure, no obstruction of the ureters. Retrograde photography revealed excellent filling of the reservoirs without retrograde flow into ureter. Most of the patients can control urination through the urinary controller, when the balloon was filled, urination stopped, when the balloon was emptied, urine passed out as a line.

CONCLUSIONS: The new procedure has advantages of self control of urination without the need of urine collecting bags or self catheterization, little disturbance on metabolism, simple surgical performance and few complications.

KEYWORDS: Urinary diversion; lieum; Reservoir; Self control; Urination

9. Honokiol, a natural plant product from magnolia tree, inhibits the bone metastatic growth of human prostate cancer cells

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BACKGROUND: Honokiol, a soluble nontoxic natural product derived from Magnolia spp., was reported to induce apoptosis in caner cells. In this study, we investigated the effect of honokiol and the combined with docetaxel on prostate cancer (PCa) growth and its bone metastasis in experimental models.
METHODS: We investigated in vitro proapoptotic effects of honokiol on human androgen-dependent and -independent PCa, bone marrow, bone marrow-derived endothelial, and prostate stroma cells. Honokiol-induced activation of caspases was evaluated by FACS analysis and Western blot. Mice bone was inoculated in vivo with androgen-independent PCa, C4-2 cells and the effects of honokiol and/or docetaxel on PCa growth in bone were evaluated. Daily honokiol (100 mg/kg) and/or weekly docetaxel (5 mg/kg) were injected intraperitoneally for 6 weeks. PCa growth in mouse bone was evaluated by radiography, serum prostate-specific antigen (PSA), and tissue immunohistochemistry.
RESULTS: Honokiol inhibited cell growth tested like above through the induction of apoptosis in all cell lines tested. In PCa cells honokiol-induced apoptosis was via the activation of caspases 3, 8, and 9, and the cleavage of poly-adenosine diphosphate ribose polymerase in a dose- and time-dependent manner. Honokiol was shown to inhibit the growth and depress serum PSA in mice harboring C4-2 xenografts in the bone and the combination with docetaxel showed additive effects that inhibited further growth without evidence of systemic toxicity. Immunohistochemical staining confirmed honokiol exhibited growth-inhibitory, apoptotic, and antiangiogenic effects on PCa xenografts.
CONCLUSIONS: The combined therapy of honokiol and low-dose docetaxel may improve patient outcome in androgen-independent prostate cancer with bone metastasis.

10. Retroperitoneoscopic nephroureterectomy with transurethral bladder-cuff excision for renal pelvic and ureteral tumors.

LIU Xiao-qiang ZHANG Gao-feng, WANG Yi, SUN Guang, et al.
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OBJECTIVE: To report our experience with retroperitoneoscopic nephroureterectomy with excision of a bladder-cuff for renal pelvic and ureteral tumors.

METHODS: Thirty-two patients (18 women and 14 men; mean age, 68 years; age range, 48-83 years) with upper urinary tract tumors underwent retro-peritoneal laparoscopic nephroureterectomy with excision of a bladder-cuff. Of the 32 cases, 12 with pelvic tumors and 20 with ureteral tumors; 17 cases had the tumors on the right side and 15 on the left. Two cases had ureteral tumors combined with bladder tumors. The needle electrode was used to circleround incise the bladder thoroughly 0.5 cm away from the ureterostoma. Three trocars in the waist were used for dissecting the kidney; and the ureter was dissected as far distally downward. Then an incision of 6 - 10 cm was created in the waist just connect 2 of the trocars to allow dissection of the distal ureter and bladder-cuff and intact specimen extraction.

RESULTS: The operation was successful in 31 patients. One case received open surgery later because of duodenal leakage. The mean operative time was 3.5 h (range, 2-6.5 h). The mean estimated blood loss was 163 ml (range, 25-1500 ml). Three cases received blood transfusion, the amount of blood transfusion was 400ml-600ml. The patient's activity recovered in 24 - 32 h after operation. Postoperative pathology showed transitional cell carcinoma in 30 cases, poorly differentiated adenocarcinoma in 1 (ureter), squamous cell carcinoma in 1(ureter). Duodenal leakage occurred in 1 patient who had had history of percutaneous nephroscope(PCN) before the operation, open surgery was done and the leakage was repaired successful. Postoperative vesical irrigation was performed to prevent tumor recurrence. The mean hospital stay was 12 d. During a mean follow-up of 15 months (range, 2-36 months), 1 patient developed pelvic and bladder metastasis after 2 months and was alive with the tumor. 1 patient developed bladder tumor after 2 years and was alive underwent TUR-BT .1 patient died of heart disease after 3months. The other 29 patients survived free of tumor to date.

CONCLUSIONS: Our data demonstrate that retroperitoneoscopic nephroureterectomy for renal pelvic and ureteral tumors has shorter incision and more rapid postoperative recovery compared with open surgery. Using resectoscope to resect the termination of ureter allows more complete excision of the ureter.

KEYWORDS: Kidney pelvis; Ureter; Carcinoma; Laparoscopy

11. Retroperitoneal laparoscopic vs open approach o nephrectomy in T1 renal cell carcinoma

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INTRODUCTION: In 1990, Clayman *et al.* [1] were the first to perform a laparoscopic radical nephrectomy for a tumor-bearing kidney. Since then, the laparoscopic approach has become widely accepted, with the benefits of decreased postoperative pain, bleeding, decreased hospital stay, and faster recovery times than with the open approach. [2–5]. We will try to demonstrate that laparoscopic radical nephrectomy could be the new gold standard treatment for renal cell carcinoma with the aid of our experiences and the current reports exploring the advantages and disadvantages of retroperitoneal laparoscopic radical nephrectomy over open surgery in T1 RCC. Reported perioperative outcomes like operating time, blood loss, postoperative analgesia requirement, and length of hospital stay and duration of convalescence had been found to be in favor of laparoscopic radical nephrectomy.

METHODS: We retrospectively analyzed the data of 352 patients who undergoing radical nephrectomy for renal cell carcinoma from Nov 2003 to Nov 2007, of these, 185 underwent retroperitoneal laparoscopic radical nephrectomy and 167 underwent open radical nephrectomy through an extraperitoneal 11th rib flank incision. Inclusion criteria comprised clinically organ-confined tumors of 7 cm or less in size without concomitant lymphadenopathy or vena cava thrombus. The operation time, hospital stay, narcotic requirement, blood loss during operation and complication after surgery were analyzed and compared. All the cases were followed up for 6-42 months and the survival rates, wound healing, and carcinoma metastasis were recorded. Oncological follow-up data were obtained from radiological reports in clinic service and phone calls to patients or their families, and were calculated from the date of surgery to the date of last appointment with physician or date of death.

RESULTS: All laparoscopic procedures were completed without open conversion. There was a statistically significant difference between retroperitoneal laparoscopic radical nephrectomy and open radical nephrectomy in blood loss, fasting period, length of hospital stay, the time to resume routine activities and total narcotic requirement after surgery; The operation time was similar in the 2 groups; All

variables (except operative duration) lower in the retroperitoneal laparoscopic radical nephrectomy group. The follow up data shows that the overall survival was 81% vs 79% (P = 0.46), and cancer-specific survival was 91% vs 93% (P =0.68), respectively.

CONCLUSIONS: Compared with open radical nephrectomy, Retroperitoneal laparoscopic radical nephrectomy is associated with lower blood loss, narcotic requirement and complications, a shorter hospital stay and earlier resumption of routine activities. Retroperitoneal laparoscopic radical nephrectomy for renal cancer confers equivalent oncological outcomes to those of open surgery. Retroperitoneal laparoscopic radical nephrectomy has become a golden standard therapy in T1 renal cell carcinoma.

KEYWORDS: Retroperitoneal laparoscopy; minimally invasive, renal cell carcinoma. Nephrectomy

12. Laparoscopic Partial Nephrectomy without renal artery control in 18 Patients with renal tumor

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PURPOSE: Hemostasis represents a primary challenge during laparoscopic partial nephrectomy (LPN). We evaluated harmonic scalpel assisted LPN without renal hilar vascular control in patients.

MATERIALS AND METHODS: LPN using harmonic scalpel was performed without renal hilar vessel control in 18 Patients with renal tumor.

The renal artery was revealed and circled by tape. So if bleeding happened, the renal artery could be controlled easily and quickly. Any defects in the collect systems were closed by sutures and seal glue. Followup involved biochemical, radiographic evaluation consisted of chest X-ray and CT or MRI of the abdomen at 1, 3, and 6 months and semiannually thereafter for 2 years.

RESULTS: All LPNs were completed successfully without open conversion and without artery control. Mean size of tumor was 3.8cm. (SD±1.5), mean operation time were 136.5 minutes (SD± 52.1) and mean estimated blood loss were 188 ml(SD±102). Preoperaton and postoperation (3Mons) serum creatinine were 85 umol/l (SD±25) and 90 umol/l (SD±27) respectively. Hospitalization days were 3.8 (SD±2.2). Pelvicaliceal suture repair was necessary in 2 of 18 kidneys (11%). In one case unexpected lymphorrhagia led to prolonged drainage time. No blood products were given intraoperatively but postoperative transfusion in one case. No positive

margin was reported. No positive result was found by radiographic evaluation in 24 months after operation.

CONCLUSIONS: Laparoscopic partial nephrectomy without renal artery control is possible especially for experienced surgeons. This skill could get a very good result for renal function recovery, blood lose and negative margin.

13. CKD as a risk factor for synchronous bladder cancer in Chinese patients with upper urinary tract urothelial carcinoma

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BACKGROUND: Some studies had reported that Chinese patients with chronic kidney disease (CKD) appeared to be at greater risk of upper urinary tract urothelial carcinoma (UUTUC). However; to date, only limited studies analyzed the clinical characteristics of the Chinese UUTUC patients with CKD. The aim of this study is to examine CKD as a risk factor for synchronous bladder cancer in a cohort of Chinese patients with UUTUC.

MATERIALS AND METHODS: Between 2005 and 2007, 161 patients (61 men and 100 women, mean age 67 years, range 37-87) underwent surgical management at our institution for pathologically proven UUTUC. We reviewed clinical, surgical, and pathological data from these patients, and used univariate and multivariate analyses to determine prognostic variables for synchronous bladder tumor. Presence of CKD according to preoperative markers of kidney damage, estimated glomerular filtration rate calculated using the Modification of Diet in Renal Disease Study equation.

RESULTS: Of the 161 Chinese patients, 20 (12.4%) had simultaneous bladder tumor and UUTT. 93 patients (57.8%) had CKD. Univariate analyses showed that patients with CKD ($p=0.008$) and the history of urothelial carcinoma ($p=0.001$) were likely to have synchronous intravesical disease; however, there was no significant impact of other factors on the synchronous intravesical disease, including age, gender, presentation (haematuria or others), tumor side, tumor location, tumor grade, lymph node metastasis. Furthermore, CKD (HR 4.042, 95% C.I. 1.271-12.855, $p=0.018$) and the history of urothelial carcinoma (HR 5.596, 95% C.I. 2.138-14.648, $p<0.001$) were identified as independent predictors for the development of recurrent bladder cancer by multivariate analyses.

CONCLUSIONS: These findings suggest that the incidence of synchronous bladder

cancer in Chinese patients with UUTUC is not very low. Concurrent CKD and the history of urothelial carcinoma are associated with greater risk of synchronous bladder cancer in these patients.

14. Clinical implication of stone culture in percutaneous nephrolithotomy

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OBJECTIVE: To evaluate the correlation between stone culture and SIRS, ascertain the clinical implication of stone culture in PCNL.

METHODS: Clinical data of 66 patients who underwent PCNL in our department were analyzed retrospectively. Eight risk factors including stone culture + drug sensitivity, urine culture + drug sensitivity, age, gender, prophylactic antibiotics, stone volume, operative time and the number of tract. Multiple statistics methods were used for analysis to evaluate the impact of SIRS, and compare the difference between stone culture and urine culture.

RESULTS: Univariate analysis and Multivariate logistic regression model showed that positive stone culture was the risk factor of SIRS ($p<0.05$). Positive stone culture was found in 48.48% patients, which was higher than that of urine culture (30.30%). Fourteen patients of 21 postoperative SIRS patients were prescribed antibiotics according to the stone culture result. And all of them recovered unevenly without developing septic shock or MODS.

Conclusions Positive stone culture is the important risk factor of post-PCNL SIRS. Stone culture is better than urine culture in directing postoperative antibiotics prescription and should be routinely used.

15. Estrogen and Selective Estrogen Receptor Modulators Inhibit Cell Proliferation in Prostate Carcinoma Cell Line PC3 Cells

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OBJECTIVE: To examine whether estrogen, tamoxifen and raloxifene have an antiproliferative effect on and stimulates the ERK1/2, JNK and p38 cascades in PC3 cells.

MATERIALS AND METHODS: PC3 cells were treated with different concentrations of 17β-estradiol, tamoxifen and raloxifene, and the method of MTT

was used to detect the inhibition rate. Morphology changes of apoptosis were observed by hoechst and TUNEL staining. The expressions of ER-α, ER-β, P21WAF1, and cyclinD1 were detected by RT-PCR. The expressions of Bcl-2, caspase-3, p-Bcl-2 and Bax were measured by immunohistochemical staining or western blot.

RESULTS : Expressions of mRNA of ER-α and ER-beta were detected in PC3 cells. A dose-dependent proliferation inhibition of 17β-estradiol, tamoxifen and raloxifene was demonstrated in PC3. Morphology changes of apoptosis were detected in PC3 cells. The expression of Bcl-2 decreased and the expression of caspase-3 increased in PC3 cells. 17β-estradiol and tamoxifen induced the activation of ERK1/2, JNK and p38 in PC3 cells with different time courses. Raloxifene could only induce the activation of ERK1/2 and p38.A G1 cell cycle arrest was induced in PC3 exposed to 17β-estradiol, tamoxifen and raloxifene. Suppression p38 activation blocked the cell-cycle arrest at the G1 phase by 17beta-estradiol.

CONCLUSIONS: 17β-estradiol, tamoxifen and raloxifene induced apoptosis and G1 cell cycle arrest via MAPK in PC3 cells.

KEYWORDS: Prostate carcinoma; Estrogen; Apoptosis; 17β-estradiol; Tamoxifen; Raloxifene