

## N65

**Survival analysis for localized low-differentiated renal cell carcinoma**

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**Introduction and Objectives:** Renal cell cancer (RCC) represents 2-3% of all malignant tumors in adults. Nuclear grading according to Fuhrman, pathological stage of primary tumors, lymph nodes metastases and presence of distant metastases at diagnosis are independent predictors of cancer-specific mortality in patients with RCC. Majority of renal tumours are diagnosed by ultrasound performed for different reasons. Despite increased detection rate survival has not improved. RCC characterized by high mortality, reaching about 40% of all surgically treated patients. To describe survival patients after nephrectomy due to low-differentiated RCC.

**Material and Methods:** A total of 40 patients with low-differentiated RCC (mean age 61.5 years), treated between January 2005 and November 2007, were included into the study. Mean observation period was 23.6 months (range from 14 to 36 months). In all cases histological confirmation of G3 or G4 RCC was received. G3 tumors were present in 31 patients (pT1b-3; pT2-9; pT3a-13; pT3b-5; pT4-1) and G4 in 9 patients (pT1b-1; pT2-3; pT3a-5). In all cases chest X-ray and abdominal CT were performed as a standard procedure. There were no metastases before surgery. After surgery all patients were followed strictly by urologist. Deaths information has been received from families and discharge cards.

**Results:** 14 patients (35%) out of 40 died during observation, including 6 (67%) out of 9 with G4 tumors (pT1b-1; pT2-2; pT3a-3) and 8 (25.8%) out of 31 with G3 tumors (pT2-1; pT3a-3; pT3b-3; pT4-1). In all cases RCC progression was the reason of death. 4 patients died in the first year after surgery, 8 patients in the second and next 2 in the third year. Metastases were found in 21 patients (52.5%) during postoperative observation. Most of them were present in lungs (12 cases, 30%) but in 7 cases (17.5%) coexisted with enlarged lymph nodes, in 2 cases (5%) with liver metastases, and in 1 case with local recurrence. Isolated bone metastases were observed in 4 cases (10%) and isolated liver metastases in 2 (5%). Among other 3 patients brain metastases, local lodge recurrence or disseminated malignant disease were found.

**Conclusions:** In spite of development in medicine and modifications in surgical technique, prognosis in low-differentiated RCC is invariable.

## N66

**Protective value of a folkloric medicinal plant extract against mortality and hemorrhage in acute renal trauma model in heparinized rats**

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**Introduction and Objectives:** We evaluated the efficacy of a folkloric medicinal plant extract (Ankaferd Blood Stopper® [ABS]) compared with oxidized cellulose (Surgicel®) in an acute renal injury model. ABS is a mixture of 5 plants that has historically been used in Turkish traditional medicine. It has been approved by the Ministry of Health to manage external hemorrhage and dental surgery bleeding in Turkey.

**Material and Methods:** Twenty-two Wistar albino rats underwent partial nephrectomy after intravenous heparin anticoagulation (2000 units per kg). The cut surface received 1 of 3 therapies, namely no treatment, Surgicel® (Johnson &

Johnson, New Brunswick, New Jersey, USA) or ABS (Trend Teknoloji İlaç A.Ş., Istanbul, Turkey). Blood pressure was continually monitored. Survival time, total blood loss and mean arterial pressure (MAP) were recorded for 60 min or until death. Rats which were alive (MAP > 20 mmHg) at the end of 60 min were sacrificed with blood withdrawal from catheters.

**Results:** All animals that received no treatment died within 60 min of follow up period. One out of 7 in Surgicel group, and 5 out of 7 animals in ABS group, survived. Mean survival times for Surgicel and ABS groups were 42.7 and 53.4 min, respectively (Table 1). Rats in the ABS and Surgicel groups survived significantly longer than rats in the control group (p < 0.05). There were no significant differences between the ABS and the Surgicel groups in survival (p = 0.128).

Table 1: Comparability of groups treated and treatment results in ABS, Surgicel and control groups

|                         | Control group<br>mean±SD<br>(n=8) | Surgicel<br>group<br>mean±SD<br>(n=7) | ABS group<br>mean±SD<br>(n=7) | p values*                 |                      |                       |
|-------------------------|-----------------------------------|---------------------------------------|-------------------------------|---------------------------|----------------------|-----------------------|
|                         |                                   |                                       |                               | Control<br>vs<br>Surgicel | Control<br>vs<br>ABS | Surgicel<br>vs<br>ABS |
| Weight (gr)             | 392.4±34.3                        | 357.3±26.4                            | 368.4±21.4                    | 0.189                     | 0.232                | 0.902                 |
| Excised Kidney (mg)     | 437.5±5.1                         | 414.3±3.78                            | 428.6±7.55                    | 0.463                     | 0.955                | 0.620                 |
| TRW% excised            | 33.3±3.4                          | 34.1±4.4                              | 32.4±3.3                      | 0.867                     | 0.694                | 0.535                 |
| BW% excised             | 0.10±0.01                         | 0.11±0.01                             | 0.11±0.02                     | 0.779                     | 0.694                | 0.805                 |
| Initial MAP (mmHg)      | 125.12±8.79                       | 130.00±10.04                          | 129.71±5.49                   | 0.536                     | 0.281                | 0.902                 |
| Final MAP (mmHg)        | 0                                 | 9.8±26.07                             | 33.28±31.25                   | 0.694                     | 0.021                | 0.097                 |
| Net Blood Loss (mg)     | 6.41±1.32                         | 6.45±1.29                             | 5.54±1.49                     | 0.955                     | 0.397                | 0.383                 |
| Net Blood Loss (mg/ kg) | 16.42±3.46                        | 18.13±3.63                            | 15.04±4.11                    | 0.397                     | 0.694                | 0.097                 |
| Survival time (minutes) | 14.25±10.45                       | 42.71±11.54                           | 53.43±13.11                   | 0.002                     | 0.001                | 0.128                 |
| Sixty-minute-survival/  | 0/8 (0%)                          | 1/7 (14.3%)                           | 5/7 (71.4%)                   | 0.467                     | 0.007                | 0.051                 |
| Total (n)(%)            |                                   |                                       |                               |                           |                      |                       |

\*Mann-Whitney U test ABS: Ankaferd Blood Stopper® MAP: Mean arterial pressure TRW % excised: The percentage of excised kidney portion to the total renal weight BW % excised: The percentage of excised kidney portion to the total body weight

**Conclusions:** ABS is as effective as Surgicel in achieving hemostasis and lengthening survival time following partial renal excision in an experimental rat model.

## N67

**RFA of the tumors in the solitary kidney**

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**Introduction and Objectives:** Along with abetter access to a better imaging technologies the number of small renal cell carcinomas (RCC), that are diagnosed has been increased. Smaller lesions are more possible to be treated with little invasive, nephron-sparing methods. Unfortunately even the most promising laparoscopic partial nephrectomy is not without drawbacks. Additionally there are more and more data that some of these small lesions may be not very aggressive. So especially in older or otherwise-not-healthy patients any aggressive techniques may appear to be not justified. This is causing that new modes of treatment such as radiofrequency ablation (RFA), that is based on thermal destruction of abnormal tissue with the heat delivered by needle probe introduced into the lesion under ultrasound control, seems to be an interesting alternative.

**Material and Methods:** We are presenting results of a treatment of 13 patients with RCC in the single kidney that have been subjected to RFA since 2003. 17 lesions were treated with 23 RFA sessions performed. The average age of the patients was 66 (55-75). The medium size of the tumor was 33 mm (21-45). Patients were qualified to this treatment because of a poor general health status or concomitant oncological disease in other organs, or because of multiple lesions in the kidney. The protocol was approved by local Ethical Committee. The tumor were diagnosed by CT with features characteristic for renal cell carcinoma. The result was assessed by CT, where no growth and no contrast enhancement were considered as a good result. Medium follow-up was 30.7 months.

**Results:** There were no complications during the RFA. In one case with multiple tumoursa ureteral stricture developed and

was later treated surgically. Size of the tumor and its localization proved to significantly influence the results. In tumors less than 30 mm in diameter good results were achieved in 89% and in tumors >30 mm in 62%. In cases with central localization of the tumor the good results were confirmed in 62% and in peripheral lesions in 89%. Minimal invasiveness of the procedure made it possible to safely repeat the treatment enabling improving the result further. Mean creatinine before was 1.31 mg/% ( $\pm 0.51$ ), and two week after was 1.43 mg% ( $\pm 0.54$ ).

**Conclusions:** In our opinion RFA of small RCC in single kidney is a valuable minimally invasive alternative to surgery. Particularly, in cases with some contraindications to the operation. Best results may be achieved in lesions smaller than 30 mm located peripherally. RFA is relatively easy and enables preservation of the functioning part of the kidney. It can be also repeated enabling to eradicate the tumor completely. Additional aspect, that has been a matter of debate recently, is that some of these small tumors may be of low malignant potential and any currently used aggressive techniques either open or laparoscopic, may be questionable, especially in old and otherwise-ill patient.

## N68

### Protective effect of caffeic acid phenethyl ester on cyclosporine A-induced nephrotoxicity in rats

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**Introduction and Objectives:** The purpose of the present study was to investigate the effects of caffeic acid phenethyl ester (CAPE) on cyclosporine A (CsA)-induced nephrotoxicity.

**Material and Methods:** Wistar-albino female rats, 250–300 g, were used in experiments. The animals were divided into four groups (n=7). In control group rats were given 0.5 ml of normal saline s.c. daily for a period of 10 days. In CAPE group rats were treated with CAPE (10  $\mu$ mol/kg/day) in 0.5 ml of normal saline i.p. daily for a period of 11 days. Rats in CsA group were injected with CsA s.c. in 0.5 ml of normal saline (15 mg/kg) once a day for 10 days. Finally in CsA+CAPE group rats were treated with CAPE (10  $\mu$ mol/kg/day) in 0.5 ml of normal saline i.p. daily for a period of 11 days and rats were s.c. injected with CsA in 0.5 ml of normal saline (15 mg/kg) once a day for 10 days beginning from the second day of CAPE administration. After the last administration of the drug, all rats fasted about 12 hours, but had free access to water. At the end of the experiment blood was collected, serum were separated and used for various biochemical estimations. The renal tissue was excised immediately from the rats, washed with pre-chilled physical saline and used for further biochemical estimations. ANOVA test was performed and post hoc multiple comparisons were made using least-squares differences.

**Results:** The administration of CsA alone resulted in higher myeloperoxidase (MPO) activity, lipid peroxidation, superoxide dismutase (SOD) and catalase (CAT) than in the control. The enzyme activities except CAT in rats treated with CAPE alone were not changed. CAPE treatment prevented the increase in malondialdehyde (MDA) and increased CAT activity more, but did not affect the activities of MPO and SOD enzymes (Table 1).

**Conclusions:** We demonstrated an increase in lipid peroxidation and MPO, SOD and CAT activity in renal tissue of rats given CsA. Additionally lipid peroxidation-mediated renal injury was prevented partly by CAPE treatment. Our results collectively suggest that CAPE may be an available agent to protect the kidney from CsA induced damage via inhibition of lipid peroxidation.

Table 1. The levels of BUN, Creatine, MDA and the activities of MPO, SOD and CAT enzymes in serum in control, CAPE, CsA and CsA+CAPE groups

|                | MDA (nmol/g protein)          | MPO (U/g protein)              | SOD (U/mg protein)             | CAT (k/mg protein)              | BUN (mg/dL)                   | Creatine (mg/dL)             |
|----------------|-------------------------------|--------------------------------|--------------------------------|---------------------------------|-------------------------------|------------------------------|
| Control (n=7)  | 8.61 $\pm$ 0.61               | 0.091 $\pm$ 0.009              | 0.284 $\pm$ 0.034              | 0.278 $\pm$ 0.028               | 15.42 $\pm$ 1.42              | 0.40 $\pm$ 0.03 <sup>a</sup> |
| CAPE (n=7)     | 10.11 $\pm$ 0.68              | 0.112 $\pm$ 0.008              | 0.353 $\pm$ 0.037              | 0.335 $\pm$ 0.005 <sup>a</sup>  | 15.14 $\pm$ 0.55              | 0.41 $\pm$ 0.04              |
| CsA (n=7)      | 11.32 $\pm$ 0.75 <sup>a</sup> | 0.126 $\pm$ 0.005 <sup>a</sup> | 0.544 $\pm$ 0.061 <sup>a</sup> | 0.361 $\pm$ 0.017 <sup>a</sup>  | 22.28 $\pm$ 1.44 <sup>b</sup> | 0.52 $\pm$ 0.03 <sup>c</sup> |
| CsA+CAPE (n=7) | 8.74 $\pm$ 0.49 <sup>d</sup>  | 0.142 $\pm$ 0.009 <sup>b</sup> | 0.687 $\pm$ 0.078 <sup>b</sup> | 0.426 $\pm$ 0.011 <sup>bc</sup> | 22.85 $\pm$ 1.31 <sup>b</sup> | 0.42 $\pm$ 0.04 <sup>c</sup> |

Results are presented as mean $\pm$ SEM; <sup>a</sup> p<0.01 compared with control group; <sup>b</sup> p<0.001 compared with control group; <sup>c</sup> p<0.05 compared with CsA group; <sup>d</sup> p<0.01 compared with CsA group; <sup>e</sup> p<0.05 compared with control group.

## N69

### Changes in peripheral blood mononuclear cells subpopulation after RFA in patients with renal cell carcinoma

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**Introduction and Objectives:** Renal Cell Carcinoma (RCC) accounts for 2–3% of adult neoplasms and about 90% of all primary renal tumors. The progress in a diagnostic technologies (USG, CT, MRI) has led to the increase in T1a tumors diagnosis. One of the most promising new treatment methods of RCC is based on high temperature created by radiofrequency current circulating around needle probe introduced into the tumor. Beside the direct destruction of the cancer tissue the treatment may induce immunologic reaction against tumor antigens released from destroyed tumor cell. The aim of this study was to evaluate the impact of RFA on the peripheral blood lymphocyte subpopulations in patients with RCC at different time points after the RFA procedure.

**Material and Methods:** Blood was tested before, and 2, 4 and 6 weeks after the RFA in nine patients with renal cell carcinoma for the proportions of CD3<sup>+</sup>, CD3<sup>+</sup>HLA-DR<sup>+</sup> (T-activated), CD3<sup>+</sup>CD4<sup>+</sup> (T-helper), CD3<sup>+</sup>CD8<sup>+</sup> (T-cytotoxic), CD56<sup>+</sup>CD16<sup>+</sup> (Natural killer) cells. The blood was stained with fluorochrome-conjugated monoclonal antibodies and percentages of cells expressing various markers were determined by flow cytometry. The tumors were diagnosed by contrast-enhanced CT. In all cases lesions were located peripherally and maximum diameter was not longer than 4 cm. In four cases RFA was performed in a single kidney (in all cases the contralateral kidney had been previously removed due to the RCC). The main reason to use RFA in these patients was the presence of medical contraindications to surgical treatment due to numerous concomitant diseases (hypertension, chronic obstructive lung disease, neurological diseases).

**Results:** Our research is for the first time showing the changes in the proportions of major peripheral blood lymphocytes subpopulations (especially CD4<sup>+</sup> and CD8<sup>+</sup>) in patients with RCC after thermoablation. In all the patients the changes were most pronounced two weeks after the RFA procedure. Interestingly, in 6 out of 9 patients the proportion of HLA-DR<sup>+</sup> T cells was increased over the whole follow-up period. The proportion of the CD56<sup>+</sup>CD16<sup>+</sup> cell cells was decreased in most of the patients. The extreme values were noted for CD8<sup>+</sup> and CD56<sup>+</sup>16<sup>+</sup> cells