616 WITHDRAWN

617 PARTIAL AND RADICAL NEPHRECTOMY FOR PT1 RENAL CELL CARCINOMA: RESULTS OF THE SATURN PROJECT

Antonelli A.[1], Novara G.[2], Simeone C.[1], Corti S.[1], Cosciani Cunico S.[1], Martorana G.[3], Minervini A.[4], Serni S.[4], Simionato A.[5], Longo N.[6], Imbimbo C.[6], Volpe A.[7], Gontero P.[8], Carmignani G.[5], Mirone V.[6], Zattoni F.[2], Ficarra V.[2]
[1]University of Brescia, Dept. of Urology, Brescia, Italy, [2]University of Padua, Dept. of Urology, Padua, Italy, [3]University of Bologna, Dept. of Urology, Bologna, Italy, [4]University of Florence, Dept. of Urology, Florence, Italy, [5]University of Genoa, Dept. of Urology, Genoa, Italy, [6]University Federico II, Dept. of Urology, Naples, Italy, [7]University of Eastern Piedmont, Dept. of Urology, Novara, Italy, [8]University of Turin, Dept. of Urology, Turin, Italy

Introduction & Objectives: To compare oncological results of elective nephron-sparing surgery (NSS) and radical nephrectomy (RN) in patients with pT1 renal cell carcinoma (RCC).
Materials & Methods: The Surveillance And Treatment Update Renal Neoplasms (SATURN) study collected the data of 5463 patients with RCC treated at 16 Italian institutions from 1995 to 2007. In the present analysis, we evaluated 3320 patients with pT1a/pT1b pN0/Nx M0 who underwent RN or elective NSS. The Kaplan-Meier method was used to calculate survival functions, and differences were assessed with the log-rank statistic. Univariable and multivariable Cox regression models addressed cancer-specific mortality.
Results: 2107 patients were male and 1113 female. Mean age at surgery was 61.3 ± 12.2 years. 1832 patients had pT1a RCC, 820 (44.8%) treated by RN and 1012 (55.2%) with NSS; 1388 patients had pT1b RCC, 1178 (84.9%) treated by and 210 (15.1%) with NSS. With regard to the pT1a cases, patients age, gender, mode of presentation, clinical and pathological tumor size, histological type, and Fuhrman nuclear grade were significantly different between patients undergoing RN or NSS (all p values ≤ 0.005). Five-year cancer-specific survival (CSS) estimates were 96.3% and 96.6% in patients treated by RN and NSS, respectively (log rank p 0.33). In Cox univariable analysis, type of surgery was not significantly associated with CSS (H.R. 0.8; p=0.33) and in Cox multivariable analysis, only age and Fuhrman grade were independent predictors of CSS in pT1a RCC. With regard to the pT1b cases, patients age, ECOG performance status, mode of presentation, clinical and pathological tumor size, histological type, and Fuhrman nuclear grade were significantly different between patients undergoing RN or NSS (all p values ≤ 0.01). Five-year cancer-specific survival (CSS) estimates were 95.6% and 94.7% in patients treated by RN and NSS, respectively (log rank p 0.78). In Cox univariable analysis, type of surgery was not significantly associated with CSS (H.R. 0.9; p=0.78) and in Cox multivariable analysis, only age, Fuhrman grade, and tumor multifocality were independent predictors of CSS in pT1b RCC.
Conclusions: Our data suggest that RN and NSS have overlapping results in terms of CSS both in pT1a and pT1b RCC. Elective NSS in renal masses larger than 4 cm may be considered as a valuable treatment in selected cases.

618 IDENTIFYING FACTORS AFFECTING RENAL FUNCTION IN PATIENTS WITH PT1B RENAL CELL CARCINOMA WHO UNDERWENT RADICAL OR PARTIAL NEPHRECTOMY

Petralia G.[1], Bertini R.[1], Capitanio U.[1], Strada E.[1], Sozzi F.C.[1], Angiolilli D.[1], Matloob R.[1], Roscigno M.[2], Carenzi C.[1], Da Pozzo L.F.[2], Bocciardi A.M.[3], Colombo R.[1], Montorsi F.[1], Rigatti P.[1]
[1]Vita-Salute University San Raffaele, Dept. of Urology, Milan, Italy, [2]Ospedali Riuniti, Dept. of Urology, Bergamo, Italy, [3]Ospedale Niguarda Ca' Granda, Dept. of Urology, Milan, Italy

Introduction & Objectives: To examine our institution experience for identifying factors affecting renal function in patients with pT1b renal cell carcinoma (RCC) treated with radical nephrectomy (RN) or partial nephrectomy (PN): still debate on a challenging issue.
Materials & Methods: From 1987 to 2007, 257 patients underwent surgery at our institution for pT1b sporadic, localized RCC, with a normal contralateral kidney (RN, n=194; PN=63). Renal function was evaluated by the estimated glomerular filtration rate (eGFR), comparing the variables to investigate the probability of renal function worsening (eGFR < 60 ml/min/1.73m^2). The outcome was evaluated and compared with Cox proportional hazards regression models.
Results: 35,6% of patients who underwent RN had renal function worsening, compared to 16% of patients undergoing PN (p=0,006). A multivariate analysis including type of surgery, age, Fuhrman grade, Charlson Index, sex, hypertension, smoking, preoperative eGFR showed significativity only for type of surgery (p=0,017) and age (p=0,001). We then stratified the cohort by year of surgery (cut-off: 1997), considering the increasing use of PN in the last decade: after 1997, only type of surgery (p=0,015) and age (p=0,011) were statistically significative, instead of hypertension (p=0,052), smoking (p=0,941) Charlson Index (p=0,495), Fuhrman grade 8p=0,384) and preoperative eGFR (p=0,490). The strong significativity of age was evident even when stratifying for age quartiles (p=0,000), with a progressive worsening of renal function through the age quartiles. Furthermore, when considering age quartiles and type of surgery, we found a significative impact on renal function only for RN (p=0,001), compared to PN (p=0,462).
Conclusions: When comparing the variables of a cohort of patients submitted to surgery for pT1b RCC, to identify risk factors for renal function worsening after surgery, the only significative factor appears to be the age. But, at further analyses, RN is the strongest risk factor: it seems that PN is a protective factor against renal function worsening when performing surgery for pT1b RCC. PN, when technically feasible and oncologically correct, represents an imperative choice for the treatment of pT1b RCC.

Poster Session 52
PROSTATE CANCER: TUMOR CELL BIOLOGY
Sunday, 20 March, 14.00-15.30, Hall I/K

619 ACTIVATED FIBROBLAST GROWTH FACTOR-INDUCIBLE 14 (FN14) PROMOTES INVASION, MIGRATION AND PROLIFERATION OF ANDROGEN INDEPENDENT PROSTATE CANCER CELLS THROUGH MATRIX METALLOPROTEINASE 9 AND CORRELATES WITH POOR TREATMENT OUTCOME

Narita S., Mingguo M., Tsuchiya N., Numakura K., Obara T., Tsuruta H., Inoue T., Horikawa Y., Satoh S., Habuchi T.
Akita University School of Medicine, Dept. of Urology, Aktia, Japan

Introduction & Objectives: Fibroblast Growth Factor-Inducible 14 (Fn14), which is a transmembrane receptor binding to a multifunctional cytokine TWEAK, has been known to modulate many cellular activities including cancer progression. Here, we demonstrated the significant role of Fn14 in invasion, migration and proliferation of androgen independent prostate cancer (AIPC) cells.
Materials & Methods: The expression of TWEAK and Fn14 in androgen-independent (PC-3 and DU145) and androgen-dependent (LNCaP) PCa cells was assessed by qRT-PCR and Western blotting. Fn14 siRNA (siFn14) and recombinant TWEAK (rTWEAK) were used for in vitro functional analyses. Cell invasiveness and migration were tested using Matrigel invasion and wound healing assays. MMP-9 activity was assessed by gelatin zymography. The effect of Fn14 on tumor growth and invasive capacity was analyzed by subcutaneous xenografts and diaphragm invasion models. Relationship between Fn14 expression in human PCa in prostatectomy specimens and clinicopathological parameters was evaluated.
Results: Fn14 and its ligand TWEAK were highly expressed in two AIPC cell lines; DU145 and PC-3, while the expression was weak in androgen sensitive LNCaP cells. Fn14 knockdown using siRNAs attenuated the migration, invasion and proliferation and enhanced the apoptosis in the two AIPC cells. Both forced overexpression of Fn14 by stable Fn14 cDNA transfection to PC-3 cells (PC-3/Fn14) and the ligand activation by recombinant TWEAK enhanced invasion in PC-3 cells. Fn14 was shown to modulate the expression and activity of matrix metalloprotease-9 (MMP-9), and the MMP inhibitor significantly reduced the invasive capacity enhanced by overexpressed Fn14. In vivo, the subcutaneous xenograft of PC-3/Fn14 significantly grew faster than that of PC-3/Mock and the invasive capacity in PC-3/Fn14 was found to be higher than that of PC-3/Mock. Furthermore, clinically, high expression of Fn14 was significantly associated with higher PSA recurrence rate in patients who underwent radical prostatectomy.
Conclusions: The Fn14 activation may contribute to multiple malignant cellular phenotypes associated with prostate cancer progression in part via MMP-9 and the Fn14/TWEAK system may be a novel therapeutic target of prostate cancer.

620 STATINS REDUCE THE RISK OF PROSTATE CANCER PROGRESSION: AN IN VITRO STUDY IN TO THE MECHANISM OF METASTASIS

Brown M.D.[1], Hart C.A.[1], Tawadros T.[1], Clarke N.W.[2]
[1]University of Manchester, Genito Urinary Cancer Research Group, Manchester, United Kingdom, [2]Salford Royal NHS Foundation Trust, Dept. of Urology, Salford, United Kingdom

Introduction & Objectives: Recent epidemiological studies have shown that although statins do not affect the overall prostate cancer risk, long term treatment (>5 years) significantly reduces the risk of advanced (especially metastatic or fatal) prostate cancer. However the mechanism of action of statins is currently unclear. The aim of this study was to utilise the in house human bone marrow stromal co-culture models to characterise the effect of statins on malignant prostate epithelial cell invasion of human bone marrow stroma.
Materials & Methods: Human bone marrow stroma was obtained with full ethical consent from patients undergoing surgery for benign disease and cultured in long term bone marrow media until haematopoietically active. All statins were used at non-toxic levels as determined by standard clonogenic assays using the PC-3 cell line. The effect of 5 statins (atorvastatin, mevastatin, simvastatin, rosuvastatin and pravastatin) on the ability of the bone metastatic prostate epithelial cell line PC-3 to invade towards, bind to and form colonies in bone marrow stroma was assessed in