Conclusions: The proteomic and epigenetic characterisation of TAF revealed specific protein and miRNA expression patterns in comparison to non-tumour fibroblasts. We observed induced expression alterations on proteomic and epigenetic level by means of co-cultivation transwell assay with tumour cells and fibroblasts. The expression changes will be also analysed in a tumour-like spheroid cell culture model. The results of this study demonstrate a strong tumour specific interplay of tumour cells and fibroblasts.

Poster Session 42
RCC: DIAGNOSIS AND PROGNOSIS
Sunday, 20 March, 12.15-13.45, Hall H

498 ACCURACY OF PERCUTANEOUS CORE RENAL BIOPSY FOR RENAL CELL CARCINOMA: ARE SUB-TYPE AND NUCLEAR GRADE CORRECTLY PREDICTED?

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Introduction & Objectives: To assess core biopsy accuracy among Renal Cell Carcinomas (RCC) by comparing preoperative and postoperative histological subtype and Führmann nuclear grade. Management of small renal masses being related to these results, correlation between accuracy and tumour size was then evaluated.
Materials & Methods: At our institution, 77 patients underwent both core renal biopsy and then surgical resection for primary RCC between February 2004 and February 2010. Percutaneous 18-gauge core biopsies were obtained under ultrasound or computed tomography guidance. According to tumour size, two groups were constituted (<4cm and ³4cm). Preoperative subtype and grade were compared with postoperative specimens results.
Results: Mean tumour size was 35.8 mm (range 10-115). Overall, biopsy correctly identified 66 out of 77 (88.0%) histological subtypes ; 5 (6.5%) primary RCC subtypes could not be defined and 6 more biopsies showed normal parenchyma (7.8%). Führmann grade was accurately assigned for 47 out of 67 (61.0%) conclusive biopsies, underestimated for 14 (18.2%) and not defined for 10 (14.9%) ($p<0.05$). Pooled with unconclusive biopsies, not less than 19 of 22 (86.4%) high grade tumours were not diagnosed by the biopsy. Tumour size had no statistically significant influence on biopsy accuracy.
Conclusions: Core renal biopsy can accurately define RCC histologic subtype. However it doesn't seem to be able to detect high grade tumours. Tumour size does not seem to influence these results.

499 CONTRAST-ENHANCED ULTRASOUND FOR CHARACTERIZATION AND FOLLOW-UP OF RENAL LESIONS

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Introduction & Objectives: The aim of the study is to evaluate the usefulness of contrast-enhanced ultrasonography (CEUS) in characterization and follow-up of renal lesions.
Materials & Methods: From March to September 2010 we performed contrast enhanced ultrasonography (CEUS) in 29 patients to evaluate 42 renal lesions. We used SonoVue (Bracco) contrast agent, MyLab 70 Gold (Esaote) and Qontrast (AMID-Bracco) dedicated software for quantification of perfusions.
Results: Overall, 37 (88%) lesions were evaluated with CEUS to better characterize previous CT scan with organojodate contrast agent (CECT) or to compare CT findings to the new method. In 4 patients with initial renal failure (5 lesions) CEUS was directly performed after standard ultrasonography (US): in this set of patients, the CEUS features were represented by suspected solid renal masses, so it was required a CECT evaluation. CEUS better defined the US features in all cases ($p=0.001$), in 20 cases (47.6%) it was adequate to characterized the lesions. In all these patients CECT confirmed CEUS findings. Overall, CEUS demonstrated a matching diagnosis with CECT in 38/42 (90.4%) lesions. In the remaining 4 cases, CT failed to show tumor blood flow in small lesions, while the CEUS capacity to quantify the perfusion demonstrated the presence of subcentrimetrical renal masses, discovered to be clear cell renal carcinoma histopathologically confirmed. Diagnostic value of CEUS resulted comparable to the CECT one, moreover CEUS was found to have an higher sensibility in characterizing small renal lesions (<1.5cm in greatest dimensions) or suspected cysts (BIIf, BIII) ($p<0.0001$). None of the patients has suffered adverse reactions to CEUS contrast agent, and no renal function worsening was suspected.
Conclusions: Contrast enhanced ultrasonography (CEUS) resulted more sensitive in detecting slight tumor blood flow than contrast enhanced CT with an improved characterization of small renal tumors. CEUS allowed a better visualization of septa number, septa and/or wall thickness, solid component and the enhancement of some renal cystic masses than standard CT. Moreover, the dedicated software (Qontrast) allowed a confirmation and a detailed definition of the observed features by the development of color maps and time-intensity curves. This safe, cost-effective procedure might be useful to better define renal lesions in patients undergoing to surgery, or to tailor an active surveillance of small masses or a postoperative follow-up avoiding organojodate contrast induced nephropathy.

500 IMPACT OF TUMOR THROMBUS CONSISTENCY (SOLID VS FRIABLE) ON CANCER-SPECIFIC MORTALITY IN PATIENTS WITH RENAL CELL CARCINOMA AND VENOUS TUMOR THROMBUS

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Introduction & Objectives: To our knowledge the impact of venous tumor thrombus (VTT) consistency in patients affected by renal cell carcinoma (RCC) has never been addressed.We analyzed the effect of VTT consistency on cancer-specific mortality (CSM).
Materials & Methods: We retrospectively analyzed 174 consecutive patients with RCC and renal vein or inferior vena cava VTT, who underwent surgical treatment surgically treated between 1989 to 2007 at our Institute. All patients underwent radical nephrectomy and thrombectomy. Pathologic specimens were reviewed by a single uropathologist. In addition to traditional pathologic features, the morphologic aspect of the tumor thrombus was specifically evaluated to distinguish solid versus friable pattern. The prognostic role of thrombus consistency (solid vs friable) on CSM was assessed by means of Cox regression models.
Results: The VTT was solid in 107 (61.5%) and friable in 67 (38.5%) patients. The presence of a friable VTT increased the risk of having synchronous nodal or distant metastases, higher tumor grade, higher pathologic stage, and simultaneous perinephric fat invasion (PFI) (all $p < 0.05$). The median follow-up was 24 months. The median CSM-free survival was 33 months. The median CSM-free survival in patients with a friable or a solid VTT was 8 and 55 months, respectively ($p < 0.001$). At multivariable analyses, the presence of a friable VTT was an independent predictor of CSM ($p = 0.02$). The power of our conclusion may be somewhat limited by the relative small study population and the retrospective nature of the study.
Conclusions: In patients with RCC and VTT, the presence of a friable thrombus is an independent predictor of CSM. If our finding is confirmed by further studies, the consistency of the tumor thrombus should be introduced into routine pathologic reports to provide better patient risk stratification.

501 EXTERNAL VALIDATION OF THE PREOPERATIVE KARAKIEWICZ NOMOGRAM IN A MULTICENTER SERIES OF PATIENTS WITH RENAL CELL CARCINOMA TREATED WITH RADICAL OR PARTIAL NEPHRECTOMY

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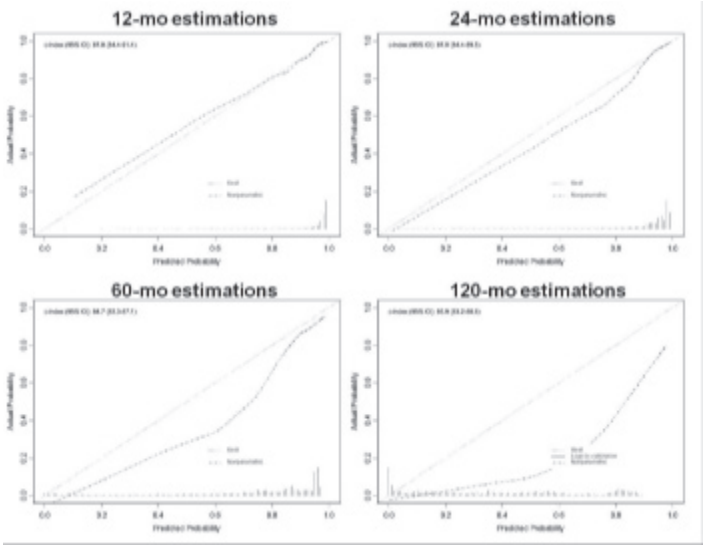
Introduction & Objectives: To validate the Karakiewicz nomogram using preoperative variables to predict cancer-specific survival of patients undergoing radical or partial nephrectomy for RCC.
Materials & Methods: We collected retrospectively the data of 3364 patients surgically treated for RCC in 16 academic centers involved in the Surveillance And Treatment Update Renal Neoplasms (SATURN) project. Univariable and multivariable Cox regression models addressed cancer-specific mortality. Concordance index was used to evaluate the prognostic accuracy of the nomogram 12, 24, 60, and 120 months after surgery.



Results: All the variables included in the nomograms (age, gender, mode of presentation, clinical tumor size, clinical T stage, presence of metastasis) were independent predictor of CSS in multivariable analysis (all p values <0.02). The prognostic accuracy of the nomogram was 87.8% (IC95% 84.4-91.4) at 12-mo; 87% (IC95% 84.4-89.5) at 24-mo; 84% (IC95% 82.3-87.1) at 60-mo; and 85.9% (IC95% 83.2-88.6) at 120-mo from surgery. Calibrations curve showed that the nomogram tended to significantly overestimate the rates of freedom from cancer-specific mortality a 60 and 120-mo, whereas the differences between estimates and observed rates at 12- and 24-mo were limited.
Conclusions: Karakiewicz nomograms has a high prognostic accuracy both in short and long term evaluation of cancer-related outcome of patients with RCC. However, according to our series, the nomograms tend to underestimate the risk of cancer-specific deaths both 60 and 120-mo after surgery.

502 EXTERNAL VALIDATION OF THE MOST ACCURATE NOMOGRAM CANCER SPECIFIC MORTALITY IN RENAL CELL CARCINOMA

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Introduction & Objectives: Accurate prediction of cancer-specific survival in patients with renal cortical tumors (RCs) is important for counselling, planning of follow-up, and selection for appropriate adjuvant trial designs. We aimed to externally validate the most accurate nomogram available (J Clin Oncol 2007, 25(11):1316-22) to predict cancer specific mortality (CSM) in RCC patients.
Materials & Methods: Clinical and pathologic data were prospectively gathered in 1170 consecutive patients treated with radical nephrectomy or partial nephrectomy at a single Academic Center, between 1991 and 2010. Nomogram predicted survival probability and actual CSM were compared. Discrimination was quantified with the area under the receiver operating characteristics curve (AUC). Calibration compared the predicted and the observed cancer rates throughout the entire range of predictions.
Results: At a median 89-month follow-up 256 renal cell carcinoma related deaths had occurred (21.9%). T classification according to TNM 2010 was pT1a, pT1b, pT2a, pT2b, pT3a, pT3b, pT3c and pT4 in 370 (31.6%), 347 (29.7%), 80 (6.8%), 44 (3.8%), 234 (20.0%), 14 (1.2%), 49 (4.2%) and 32 (2.7%), respectively. Mean pathological diameter of the tumor was 6.1 cm (median 5.0 cm, range 1-23). At nephrectomy lymph node and distant metastases were present in 83 (7.1%) and 182 cases (15.6%), respectively. Grade 1-2 or 3-4 was noted in 824 tumors (70.4%) and 346 (29.5%), respectively. Thirty-seven (3.2%) and 80 (6.8%) patients showed local and systemic symptoms at diagnosis, respectively. One, 2, 5 and 10-year cancer specific survival rates were 91.9%, 87.2%, 79.3% and 72.9%, respectively. For nomogram-derived CSM-free survival predictions at 1 to 10 years, the accuracy of the nomogram ranged from 85.5 to 91.1%. The calibration between the predicted and observed recurrence-free survival rates was virtually perfect at 1 to 5 years after nephrectomy with slightly departures between the predicted and observed rates between 5 and 10 years after nephrectomy.
Conclusions: We externally validated a highly accurate tool specifically for renal renal cell carcinoma to predict disease specific survival. This nomogram resulted the most accurate tool to identify renal cell carcinoma with aggressive clinical behavior and may contribute to the ability to individualize postoperative surveillance and therapy.

503 HEAD-TO-HEAD COMPARISON OF THE MOST RELEVANT INTEGRATED PROGNOSTIC SYSTEMS PREDICTING CANCER-SPECIFIC SURVIVAL IN CLEAR CELL RENAL CELL CARCINOMA

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Introduction & Objectives: To compare the performances of UISS, SSIGN score, and Karakiewicz nomogram in a large multi-institutional series of patients with clear cell RCC.
Materials & Methods: We collected retrospectively the preoperative, pathological and follow-up data of 1871 patients treated in 16 academic centers. The predictive accuracy of the three prognostic models for prediction of CSS was quantified according to Harrell's concordance index, whereas differences were estimated using the DeLong test. Decision curve analyses were used to determine the optimal benefit derived from the use of the 3 models.
Results: At a median follow-up of 40 months, 272 (15%) had died of disease. Overall 3- and 5-year CSS estimates were 87.5% and 83.1%, respectively. The predictive accuracy estimates for prediction of CSS at 3 and 5 years were 88.9% and 88.8% for the Karakiewicz nomogram; 85.0%, and 84.1% for the UISS; and 87.9% and 82.5% for the SSIGN score, respectively. Most of the differences in predictive accuracy were statistically significant. Calibration plots demonstrated substantial departures from ideal predictions for all the model. The Karakiewicz nomogram demonstrated the highest net benefit up to threshold probability of 25% and 37% at 3 and 5 yrs, respectively. Following those thresholds, the UISS resulted with the highest net benefits.
Conclusions: All three models demonstrated substantially sensible predictive accuracy, but all tend to underestimate the CSS probabilities. The Karakiewicz nomogram demonstrated the highest net benefit up to threshold probabilities of 25% at 3 yr and 37% at 5 yr, whereas, the UISS resulted with the highest net benefit in patients with higher risks of deaths.

504 STAGE-PER-STAGE ANALYSIS OF AGE AND CANCER-SPECIFIC MORTALITY (CSM) IN PATIENTS WITH RENAL CELL CARCINOMA (RCC): A RETROSPECTIVE ANALYSIS

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Introduction & Objectives: Controversy exists in the management of elderly patients with RCC. Some reports suggest that in these patients, surgical treatment may actually cause harm, while others disagree. We sought to test this hypothesis in a large population-based North American cohort.
Materials & Methods: Between years 1988 and 2006, 36333 RCC patients treated with partial or radical nephrectomy (RN) were identified within the Surveillance, epidemiology and end results database. Patient age was stratified into decades: <50 vs. 50–59 vs. 60–69 vs. 70–79 vs. ≥80 years old. Disease stage was defined according to the AJCC/TNM staging system: stage I vs. stage II vs. stage III vs. stage IV. Tumor grade was defined low (I–II) vs. high (III–IV). Cox regression analyses were performed for prediction of CSM in the entire population, then repeated according to AJCC stage and grade categories. Finally, we repeated our analyses in patients treated with exclusively RN.
Results: Respectively 18, 25, 27, 23, and 7% of patients were aged <50, 50–59, 60–69, 70–79, and ≥80 years. Most patients were white (82%), underwent a RN (80%), clear cell (89%), low grade (74%), and stage I (67%). After adjusting to all covariates, persons aged ≥80 years had a higher rate of CSM than their younger counterparts (hazard ratio [HR]: 2.3, P<0.001). This effect was consistent in the stage per stage analysis: stage I HR: 5.1, P<0.001 vs. stage II HR: 2.0, P<0.001, stage III HR: 1.8, P<0.001, stage IV HR: 1.7, P<0.001. Following stratification of patients according to stage and grade categories, the effect of worse survival in octogenarians persisted across all categories. Furthermore, this finding remained unchanged in patients treated with exclusively RN.
Conclusions: More advanced age is an independent predictor of higher CSM across all stage and grade categories after nephrectomy. In consequence, surgical management of the elderly in RCC patients may not represent the ideal treatment option. Further studies are needed to confirm these results.