Podium Session 5: General Oncology & Late Breaking Abstracts June 25, 2013, 0840-0940

POD-05.01

Contrast-enhanced Ultrasound of Solid Renal Masses: Non-invasive Discrimination between Renal Cell Carcinoma and Benign Renal Tumours

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Introduction and Objectives: Contrast-enhanced ultrasound (CEUS) is an emerging imaging modality for the diagnostic workup of renal masses. CEUS avoids ionizing radiation and contrast-related toxicity associated with conventional imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI). We evaluated the utility of CEUS in predicting the histopathology of solid renal masses.

Methods: We assessed the ability of CEUS to predict tumour pathology in 32 solid renal masses in 31 patients (mean age 65 years) undergoing extirpative therapy at our institution. The presence of four main CEUS characteristic were evaluated in each mass including level of arterial enhancement compared to adjacent renal parenchyma (either hypoenhancment, isoenhancement, or hyperenhancement), enhancement pattern (either homogenous or heterogeneous), washout, and peri-lesional rim enhancement. Two radiologists assessed radiographic findings. The findings for each mass were compared with surgical pathology in order to determine predictive CEUS characteristics.

Results: Our series consisted of 24 renal carcinomas (19 clear cell, 3 chromophobe, and 2 papillary tumours) and 8 benign tumours (6 oncocytomas, 1 angiomyolipoma and 1 metanephric adenoma). Mean tumour size was 3.1 cm (range 1.2 to 5.7cm). Heterogeneous enhancement alone had a 94% positive predictive value (95% CI 69-99), 44% negative predictive value (95% CI 19-70), 63% sensitivity (95% CI 40-81) and 88% specificity (95% CI 47-99) in predicting malignancy. The combination of isointense or hyperintense enhancement and homogeneous enhancement had a 67% positive predictive value (95% CI 29-92), 91% negative predictive value (95% CI 71-98), 75% sensitivity (95% CI 34-96) and 88% specificity (95% CI 67-97) for a benign tumour.

Conclusions: Our early experience with CEUS in the evaluation of solid renal masses demonstrates good accuracy in discrimination between malignant and benign tumours. This non-invasive diagnostic modality appears to be better than CT or MRI and may be comparable to percutaneous biopsy. Our initial results have prompted a larger corroborative prospective trial to evaluate the diagnostic accuracy of CEUS in predicting pathology in renal masses. CEUS may have an important role in the management of small renal masses.

POD-05.02

External Validation and Creation of a new Classification Tree for the Prediction of Benign Versus Malignant Disease in Patients with Small Renal Masses

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Background and Objectives: The preoperative prediction of benign disease remains a significant challenge for the urologist. We have published a classification tree to preoperatively predict benign vs. malignant disease of small renal masses (SRM's) with 89% accuracy. The objectives of this study were to externally validate our classification tree in a different cohort, to create a new classification tree combining the 2 cohorts and to determine if the R.E.N.A.L. or PADUA scoring systems predict malignancy.

Methods: This study includes 591 patients with renal masses. 395 from Halifax, Canada had surgical resection of their renal mass. Age, sex, volume on preoperative imaging, tumour location (central/peripheral), degree of endophytic component (1-100%), and tumour axis position were used to develop a classification tree for the prediction of benign disease. 196 patients from Toronto, Canada had renal biopsies followed by Active Surveillance, Radiofrequency Ablation or surgical resection of their mass.

Results: When externally validated with the Toronto cohort, the predictive accuracy of the Halifax classification tree dropped from 89 to 73%. A new tree built using the Toronto cohort only, showed an accuracy of 79.5% (95% CI: 72.4, 85.5). By combining the Toronto and Halifax cohorts a tree was created with a predictive accuracy of 86% (95% CI: 83, 88.9). When validated with the Toronto and Halifax cohorts alone the accuracy is 79 and 89% respectively. Neither the R.E.N.A.L. or PADUA scoring systems were predictive of malignancy in the Toronto cohort.

Conclusions: A classification tree built on two cohorts has a better predictive value than the classification trees created with each individual cohort. This tree has a predictive value greater than currently published nomograms and biopsy cohorts.

POD-05.03

Association of Male Pattern Baldness and Risk of Cancer and High Grade Disease Among Men Presenting for Prostate Biopsy

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Background: Androgens have been implicated in both male pattern baldness (MPB) and prostate cancer. We set out to prospectively determine if men with independently assessed MPB are at higher risk for prostate cancer at biopsy and determine if any grade associations exist.

Methods: We prospectively enrolled 320 eligible patients presenting for prostate biopsy and independently determined their MPB pattern using the validated Norwood classification (0 no balding; 1 mild vertex balding; 2 moderate vertex balding and 4 severe vertex balding) system. Univariate and multivariable models including Norwood score, age, prostate-specific antigen (PSA) and digital rectal examination (DRE) abnormalities were calculated for the outcomes of cancer and high-grade disease (Gleason >6). C-statistics analyses of our models were then compared with and without MPB pattern for marginal utility.

Results: Of the 320 participants, 182 patients (57.7%) had cancer and 106 patients. (33.6%) had Gleason 7 disease or higher. Total cohort median PSA was 5.8 ng/ml, mean age was 63.9 years and 25.8% had DRE anomalies. On univariate analyses, Norwood patterns were increasingly associated with cancer and high grade disease with a dose-effect (P for trend <0.0001for cancer and p=0.0036 for high grade disease). On multivariable analyses, trends still held with all patients exhibiting Norwood scale 2 or higher at increased risk for cancer (Norwood 2 OR 2.77 [p=0.0159]; Norwood 3 OR 2.73 [p=0.0137]; and Norwood 4 OR 5.40 [p<0.0001]) . In predicting risk of high-grade disease, only patients with Norwood pattern 4 (Norwood 4 OR 3.05 [p=0.0052]) exhibited an increased risk, although trends persisted for lesser MBP scores (p for trend=Norwood 2 OR 2.77 [p=0.0159]) (Norwood 2 OR 2.77 [p=0.0159] 0.0036). Age and DRE abnormalities were also associated with cancer and high-grade disease.
Conclusion: MPB appears to be a strong and independent risk factor for prostate cancer and high-grade disease.

POD-05.04

Initial Results of MR Guided Laser Focal Therapy for Prostate Cancer

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Introduction and Objectives: Novel treatment strategies for prostate cancer (PCa) are being explored. We report the first comprehensive safety study and initial biological response to MRI guided and controlled laser focal ablation (MRgFLA) in men with PCa.
Methods: 38 men with low-intermediate risk, organ-confined PCa were treated between 2010 and 2012. MRgFLA was performed with the patient in the bore of an IMRI. Laser fibers were placed within the prostate via the perineum under MR imaging guidance. MR thermometry sequences provided realtime information on the ablation. Response was assessed using post-procedure MRI and 4 months TRUSBX. Adverse event recording and patient-reported outcome measures were collected.
Results: 40 procedures were carried out in 38 men. Median follow-up 538 days. 64% had Gleason 6, 36% Gleason 3+4. MRgFLA was feasible in all men. The procedure was done on an outpatient basis in all cases. No intra-procedure complications were encountered. Of the 34 who have had a biopsy 16 (47%) had a negative biopsy following the procedure, 9 (26%) had a negative biopsy in ablated quadrant but positive in contralateral lobe. 8 out of the 10 patients with Gleason 3+4 who have had a biopsy were negative. Post-procedure complications included 3 Clavien 1 complications (urinary retention). 31 of the 32 patients with mild or no erectile dysfunction prior to the procedure (96%) maintained potency after the procedure without using PDE5I.
Conclusions: MRgFLA is a safe outpatient procedure with minimal morbidity. The initial biologic response suggests that the targeted tumour can be completely ablated in 75% of cases. MRgFLA appears equally effective for Gleason 3 + 3 and 3+4 disease. Future enhancement of imaging and targeting of aggressive tumour foci are likely to yield improved results. This treatment may offer a significant benefit in the form of reduced morbidity for those men desiring elimination of their MR visible focus of cancer. Further trials will determine the true oncologic utility of MRgFLA.

POD-05.05

Effects of Tadalafil (TAD) Treatment on Erectile Function Recovery Post-bilateral Nerve-sparing Radical Prostatectomy (nsRP)

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Introduction and Objectives: The possible rehabilitative impact of following nsRP on penile function remains unclear. This multicentre, randomized, double-blind, double-dummy, placebo (PLC)-controlled trial (NCT01026818) primarily assessed the proportion of patients achieving an IIEF-EF score ≥22 after 6 weeks (w) washout. Secondary measures included IIEF-EF, Sexual Encounter Profile question 3 (SEP3) and penile length (PL).
Methods: Patients ≤68 years with adenocarcinoma of the prostate (Gleason ≤7) and normal preoperative EF were randomized 1:1:1 to either a 9-month treatment of TAD 5mg once a day (OaD), TAD 20 mg on demand (pro re nata, PRN) or PLC post-nsRP, followed by a 6-week washout phase and a 3-month open-label phase on TAD OaD (all patients). Logistic regression and ANCOVA adjusting for treatment, age and country were applied to IIEF-EF ≥22, SEP3 and PL.
Results: 423 patients were randomized to TAD OaD (N=139), TAD PRN (N=143) and PLC (N=141). Mean (SD) age was 57.9 (5.58) years. 20.9% of patients in the TAD OaD, 16.9% in the TAD PRN and 19.1% in the PLC arm reached an IIEF-EF ≥22; odds ratios (95% CI) for TAD OaD and TAD PRN vs. PLC were 1.14 (0.63, 2.06; p=0.675) and 0.89 (0.48, 1.65; p=0.704). IIEF-EF and SEP3 improved more during the double-blind phase in patients actively treated, where only TAD OaD vs. PLC was significant, decreased during washout, but further improved during open-label treatment (numerically best for patients randomized to TAD OaD). PL reduction after the double-blind phase was significantly lower vs. PLC in the TAD OaD arm only (LS mean; 95%CI: 4.20; 0.47, 7.93; p=0.028). Treatments were well tolerated with no unexpected safety signals.
Conclusions: Improvements in EF gained during 9m of active treatment with TAD were not maintained after a 6w washout. However, TAD OaD given early after nsRP suggests advantages versus delayed treatment in responsiveness to treatment and in protecting from structural penile impairment post-nsRP.

POD-05.06

Nadir Testosterone on ADT Predicts for Time to Castrate Resistant Progression: A Secondary Analysis of the PR-7 Intermittent vs. Continuous ADT Trial

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Background and Rationale: The continuous arm of the PR-7 study, consisting of more than 600 patients on long term ADT followed prospectively for a median of 8 years, represented an ideal opportunity to address the

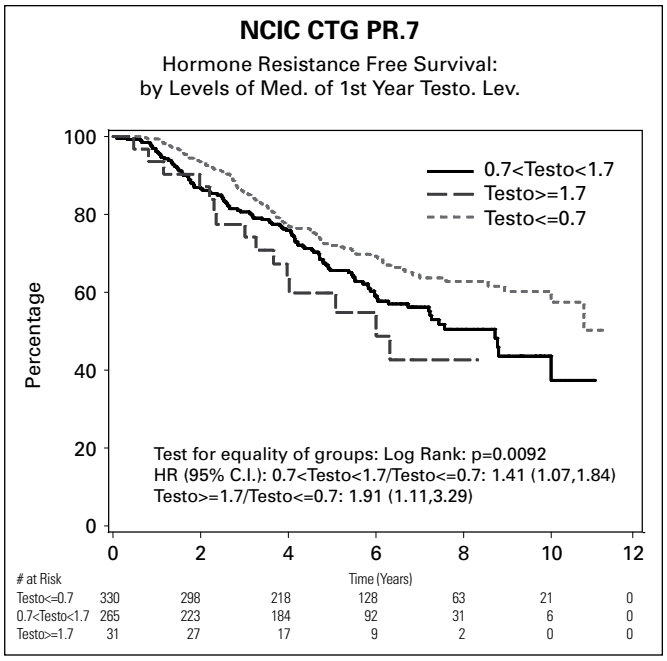

Fig. 1. POD-05.06.

importance of nadir Testosterone with respect to disease progression.

The primary hypothesis was that higher castrate testosterone values while on CAD correlate with a reduced time to development of castrate resistant prostate cancer (CRPC) and lower CSS. All patients randomized to CAD arm of PR7 trial are included, excluding only those who did not actually receive CAD or had inconsistent dosing.

Eligible patients in the PR7 trial had had previous radiation as primary therapy, or surgery with radiation for initial PSA recurrence, with a rising PSA >3, serum T >5 nmol/L, and a negative bone scan. Patients were randomized 1:1 between IAD and CAD. Serum Testosterone was evaluated 3 times in the first year after treatment was initiated. Groups were analyzed according to median and maximum serum T <0.7, 0.7-1.7, and ≥1.7 nMol/L. 626 men were included in this analysis.

Results: Amongst the 626 evaluable patients, 53% achieved a median T < 0.7; 41% between 0.7 and 1.7; and 5% ≥1.7 nM/L. Maximum T was <0.7 in 27%, 0.7-1.7 in 50%, and ≥1.7 in 23%. The median and maximum testosterone levels were significantly associated with patients' age (lower T in older patients).

226/626 developed hormone resistant disease. The median time to hormone resistance was 10.0 years (95% C.I. 8.72 to not estimable). The 5-year event free rate was 69% (95% C.I. 65 to 72%).

Nadir testosterone predicted for (p=0.009) time to hormone resistance. Patients with higher T had a significantly higher risk of developing hormone resistance (for serum T between 0.7 and 1.7, HR 1.41 (CI 1.07-1.84); and serum T ≥1.7, HR 1.91 (CI 1.11-3.29). Maximum Testosterone >0.7 (reflecting breakthrough) trended to more rapid progression to hormone resistance, but this did not achieve significance (p=0.17, HR 1.2 and 1.4 for serum T >0.7 and ≥1.7). Cause specific survival was not significantly different between the groups (Fig. 1).

Conclusion: This study demonstrates conclusively that low nadir serum Testosterone on ADT <0.7 mMol/L correlates with improved duration of response to androgen deprivation in men on CAD being treated for biochemical failure. Serum Testosterone should be assayed regularly on such patients, and ADT modified to ensure levels <0.7 are achieved.