BJUI

BAUS Annual Meeting, 15–18 June 2015

Best Academic Paper Session

Monday 15 June
Best Academic Paper Session
0900–1000 Charter 1
BEST ACADEMIC PAPER SESSION
Chair: Professor Rob Pickard
Papers 1–6

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1

The role of pre-operative histology in nephroureterectomy: The UK experience

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Introduction: There is on-going debate about the role of pre-operative histological diagnosis of TCC prior to nephroureterectomy. Some Urologists would favour this option. Others would be happy to proceed with nephroureterectomy on the basis of pre-operative imaging. A single study has underlined the importance of obtaining a pre-operative histological diagnosis. This study reviews the UK experience in the surgical management of upper tract TCC, and evaluates the significance of pre-operative histological diagnosis.
Materials and Methods: The BAUS nephroureterectomy database (years 2012 & 2013) was reviewed. 2018 nephroureterctomies were recorded in BAUS database. Post-operative histology was not recorded in 82 cases. Nephroureterectomy for benign reasons was performed in 40 cases. Both subgroups were excluded of the study (n = 1896 patients).
Result: Pre-operative histological diagnosis and/or abnormal urine cytology were obtained in 358 patients before undergoing nephroureterectomy (Group-1). Interestingly, 8 out of the 358 patients had benign final histology despite a pre-operative histological diagnosis of TCC (4 patients) and abnormal urine cytology in the other four.
Patients in group-2 (1538 patients) underwent nephroureterectomy based on pre-operative imaging only. 12 (0.8%) patients had benign post-operative histology. 84% of patients had TCC in their surgical specimen (Table 1).
54 (4%) patients had G1 disease. 18 (1%) of the 54 patients had less than 2 cm tumour.
Conclusion: Surgical management of upper tract TCC varies in the UK. Majority of cases are performed with no pre-operative histological diagnosis (81%). The incidence of benign histology is extremely low in these patients whether or not they had biopsy.

Table 1 (Paper 1).

Post-operative histology	Group 1	Group 2
TCC	341 (95.3%)	1291 (84%)
RCC	1 (0.3%)	95 (6.2%)
Papillary	4 (1.1%)	43 (3%)
Other cancer	4 (1.1%)	40 (3%)
Benign	8 (2.2%)	12 (0.8%)
Incomplete histology	0	47 (3%)

2

24-Month functional results of a prospective randomized controlled study comparing greenLight XPS to TURP for durability, efficacy and safety (GOLIATH)

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Introduction: Recently published six and twelve-month results from Goliath have demonstrated non-inferiority of GL-XPS by IPSS at 6-months and durability of results at 12-months. We now report 24-month outcomes demonstrating long-term durability for the treatment of LUTS/BPO.
Methods: 291 patients were enrolled at 29 sites in 9 European countries. Patients were randomized 1:1 to undergo GL-XPS or TURP. The trial was powered and designed to assess non-inferiority of GL-XPS compared to TURP. Patients were evaluated at 6, 12 and 24-months. Several objective and subjective parameters were assessed at 24-months (IPSS, IPSS-Qol, Qmax, PVR, prostate volume and PSA).
Results: After one year, 92.6% of the 269 treated patients remained in the trial (128 GL- XPS and 121 TURP). The endpoints of IPSS, Qmax, IPSS-Qol, PVR, prostate volume and PSA were not statistically different between treatment arms overall. The proportion of patients who were complication free was 83.6% in GL-XPS and 78.9% in TURP. Measures of safety,

efficacy and quality of life (IIEF-5, IPSS-Qol, PVR, prostate volume and PSA) were not statistically different between treatment arms.
Conclusions: GL-XPS and TURP show comparable safety, efficacy and quality of life results after 24-month follow-up. GL-XPS remains non-inferior to TURP in terms of IPSS, Qmax and complication free rate. GOLIATH data demonstrates a similar level of durability for GL-XPS and TURP.

3
Altered expression of markers of epithelial-to-mesenchymal transition at the extraprostatic extension component of locally invasive prostate cancers

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Introduction: Epithelial to mesenchymal transition (EMT) describes the loss of epithelial cell properties such as cell polarity and cell-cell adhesion, and the gain of migratory and invasive behaviours normally seen in mesenchymal cells. EMT has been described in many adenocarcinomas including prostate cancer however it is unclear whether EMT occurs in specific areas of primary prostate cancers such as the extraprostatic extension component of pT3 disease. We tested the hypothesis that proteins previously described as regulators of EMT may have altered expression and/or sub-cellular localisation at the extraprostatic extension component of prostate capsule-invading pT3 tumour samples. We also investigated the possibility that *in vitro* prostate cancer cell organotypical cultures might demonstrate changes in EMT-related protein expression at the 'leading edge' of cellular invasion.
Material and Methods: Whole mount sections of 27 cases of pT3a prostate cancer treated by radical prostatectomy were chosen so as to include the focus of invasion of the prostatic capsule. Sections were stained for eleven candidate EMT-related proteins (E-Cadherin, Twist, Snail, Fibronectin, N-Cadherin, α smooth muscle actin, Vimentin, β-catenin, SHH, Gli-2 and NFκB p65). PC3, DU145 and LNCaP prostate cancer cells were grown for 10 days as *in vitro* organotypical cultures on gel plugs containing 1:1 collagen/Matrigel (C) and normal human fibroblasts, before being fixed in formalin, processed and sectioned for histology. The nuclear, cytoplasmic and membranous expression of each protein in extraprostatic extension tumour, intra-prostatic tumour, and histologically benign cells in pT3 sections was quantified by a uropathologist. A similar semi-quantitative expression analysis was performed for cells at the invasive 'leading edge' of the *in vitro* organotypical cultures compared with the upper non-invasive edge.
Results: The expression profiles of five markers of EMT (E-Cadherin – reduced membranous, increased cytoplasmic; Twist – increased nuclear and cytoplasmic; Snail – reduced membranous; α smooth muscle actin – increased cytoplasmic; and NFκB p65 – increased nuclear and cytoplasmic) were significantly different in the extraprostatic extension component of pT3 prostate cancer compared with the intra-prostatic tumour ($P < 0.05$ for each). No significant differences were observed for Fibronectin, N-Cadherin, Vimentin, SHH, Gli2 and β-catenin. Three of these significantly altered EMT-related proteins (increased cytoplasmic α–smooth muscle actin, decreased membranous E-cadherin, and increased cytoplasmic Twist) exhibited the same significantly altered expression pattern in PC3 cells grown in organotypical culture.
Conclusions: Taken together these results suggest that EMT-like changes in protein expression can be observed within the extraprostatic extension component of locally invasive prostate cancers. Moreover, the biological significance of at least some of these observed changes in protein expression may be studied in *in vitro* cell culture models.

4
Workplace patterns and urothelial bladder cancer phenotype – can occupation increase the risk of developing advanced disease?

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Introduction: Urothelial Bladder cancer (UBC) is a common malignancy that can arise from occupational carcinogen exposure. Recent next generation sequencing studies (TCGA) have shown that muscle invasive UBC comprises distinct sub-sets of tumours. We hypothesized that the proportion of non-invasive and invasive UBC, (and disease specific mortality [DSM]), could vary between occupations where workers maybe exposed to different carcinogens triggering a specific disease phenotype.
Patients: We examined UBC incidence, stage at diagnosis and DSM in 1.7 million men (with 13 717 UBCs) and 1.7 million (with 4282 UBCs) women (follow up of 37 and 43 million person years, respectively) with annotated occupational descriptions. We identified DSM in 3615 (26% out of incident UBCs) males and 1414 (33%) females.
Results: Incidence of 'advanced' tumours was higher than in the comparable population for male seamen (standardized incidence ratio 2.15, 95% confidence interval 1.25–3.44), welders (1.86, 1.12–2.90) and miscellaneous construction workers (1.44, 1.10–1.85), and in female construction workers (2.71, 1.00–5.90), and waiters (2.27, 1.30–3.68). Fewer than expected advanced tumors were observed in male teachers (0.53, 0.30–0.86), military personnel (0.17, 0.00–0.94) and chemical process workers (0.24, 0.05–0.71. Higher than expected DSM rates were seen in male building caretakers (1.39, 1.09–1.76), transport workers (1.27, 1.01–1.59), the economically inactive (1.24, 1.14–1.35) and engine operators (1.23, 1.00–1.49), and in female assistant nurses (1.55, 1.01–2.27) and hairdressers (1.99, 1.03–3.47).
Conclusion: We have identified occupations with different risks for bladder cancer phenotype and for DSM. Further work is needed to identify candidate carcinogens that may account for the observed differences.

5
Multilocular cystic renal cell carcinoma has an excellent prognosis regardless of size or pathologic T-stage: Results of a large population-level study

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Introduction: Renal cell carcinoma (RCC) makes up 3–5% of all cancers, with

cystic-RCCs in 3–14%, detected as complex enhancing renal cysts on imaging. Since 2004, pathological reclassification led to description of multilocular-cystic-RCC (mcRCC) and tubulocystic-RCC.
Aims: To study histologic patterns, survival outcomes of cystic RCCs using a province-wide cancer-registry-database.
Material and Methods: Retrospective review of all histologically-proven cases of cystic-RCC treated by partial or radical nephrectomy (PN/RN) between 1995–2008 identified from Ontario Cancer Registry. Patient demographics, surgery type, histologic features, survival outcomes evaluated. Cystic necrosis was excluded.
Results: 168 cases of cystic RCCs were identified. Mean age 54.5 yrs, males 58%. RN was performed in 58% with adrenalectomy in 25%. Mean lesion size 4.1 cm (1–18 cm). Vast majority cystic-clear-cell or multilocular-cystic-RCC (mcRCC), 1 tubulocystic RCC. 98% low grade 1–2. No adrenal involvement where removed. All cases were margin-negative. Median post-operative follow up of 9.75 years. Thirty deaths occurred but only 3/168 reported from cancer (cancer-specific survival 98%). No difference in survival outcome based on T-stage or tumour size noted.
Conclusion: Largest series of cystic RCCs to date confirms an excellent prognosis of mcRCC, making a strong case for nephron-sparing, adrenal-saving approach for cystic renal masses suspicious of being RCCs. Magnitude is underrepresented as only proven cancerous cysts reported. We also confirm that size of the cystic renal cancer makes no difference to outcomes. We opine that labelling a 10 cm mcRCC as T2 is erroneous as tumour burden is much less than similar sized solid RCCs. We therefore propose that true cystic RCCs should not be pT-staged.

6
Exploring the potential of Fluorine-18 fluorodeoxyglucose positron emission tomography (18F-FDG PET) to improve clinical decision making in patients with Retroperitoneal fibrosis (RPF)

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Introduction: Clinical decisions in RPF are often difficult. Is the RPF malignant? Might the RPF be part of a systemic process? When should steroids be started/stopped? Who should have ureterolysis? How can patients be safely monitored? The degree of metabolic activity/inflammation within the RPF has the potential to influence these decisions and led us to explore the value of CTPET in managing RPF.
Methods: Prospective study of 73 patients evaluated by a multi-disciplinary RPF team since February 2012. 35 of these underwent PET in addition to CT and blood tests.
Results: 2/2 patients with malignant RPF had marked avidity on CTPET in non-typical areas for RPF
Biopsy of FDG-positive lung mass led to diagnosis of ANCA-positive vasculitis
23/35 (66%) positive PET
- 17/23 (74%) raised markers*
- 6/23 (26%) normal markers*

12/35 (34%) negative PET
- 5/12 (42%) raised markers*
- 7/12 (58%) normal markers*

8/23 (35%) patients with positive PET and 2/12 (17%) with negative PET showed a response to steroids with shrinkage of the retroperitoneal mass
10/23 (43%) with positive PET had pain compared to 2/12 (17%) with negative PET
*CRP and ESR
Conclusion:
1. PET may help diagnose malignancy in patients thought to have idiopathic RPF
2. PET may detect metabolic activity in RPF when inflammatory markers are normal
3. Where inflammatory markers are raised but the PET is negative, alternative causes should be sought
4. Patients with positive PET are twice as likely as those with a negative PET to respond to steroids

The use of PET in RPF remains investigational but has the potential to enhance clinical decision-making and is worthy of further study.