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POD-5.01

Treatment trends for renal cell carcinoma in a population-based tumour registry: the potential underuse of partial nephrectomy

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Introduction and Objective: Recent evidence suggests that renal function correlates with cardiac morbidity and overall survival. However, nephron-sparing approaches such as partial nephrectomy (PN) may be infrequently used in the treatment of renal masses, particularly in the elderly. We examined population-based trends for renal cell carcinoma (RCC) management over a 10-year period.

Materials and Methods: We identified 7830 patients treated surgically for RCC in the province of Ontario, Canada between 1995 and 2004 using the Ontario Cancer Registry, a population-based tumour registry. Demographic, treatment and vital status information was obtained for all patients. A multivariable logistic regression model was used to determine predictors of PN use. A survival analysis was used to estimate disease-specific and overall survival.

Results: The mean age of patients was 60 years, of which 4826 (61.6%) were men. Of these, 7042 (90%) were treated with radical nephrectomy (RN) and 788 (10%) with PN. There was a significant decrease in PN use with increasing age; 11.8% of patients younger than 50, compared with only 4.9% of patients 80 and older ($p < 0.0001$). An increase in PN usage was observed from 1995 to 2002, however a plateau was noted with increasing laparoscopic RN use in recent years. Laparoscopic procedure codes were implemented in 2002, and thereafter an increasing proportion of procedures were performed using this approach; 48 cases in 2002 compared with 296 in 2004. On multivariable logistic regression, age ($p < 0.0001$) and year of surgery ($p < 0.0001$), but not gender, were independently associated with PN use. The unadjusted 5-year cancer-specific and overall survival estimates were 86.1% and 71.2%, respectively.

Conclusion: Although previously hypothesized, this is the first evidence on a population level suggesting that laparoscopic RN may have impacted adversely on the uptake and application of PN to RCC. The infrequent use of nephron-sparing surgery is especially evident in the elderly, who may benefit the most from this approach. There is a need for further education of urologists about the importance of nephron-sparing surgery in RCC.

POD-5.02

How long can patients with renal cell carcinoma wait for surgery without compromising pathological outcomes?

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Introduction and Objective: Surgical wait times have been shown to be of significance in other malignancies (such as bladder cancer), but limited studies exist in renal cell cancer (RCC). Despite the lack of evidence, government agencies, such as the Ontario Ministry of Health and the National Health Service (NHS) in the United Kingdom have recommended no more than 4 weeks waiting time for surgery for RCC. We analyzed surgical waiting time for RCC patients to see if there was an adverse impact on pathological characteristics.

Materials and Methods: Our centre triages the RCC patients on the basis of perceived tumour risk. The waiting time for surgery is stage for stage: clinical T1 90 days, T2 40 days, T3 and T4 30 days. We retrospectively reviewed the charts of 351 patients who underwent surgical resection for RCC. Evaluable patients were assessed for pathological upstaging, positive lymph nodes, tumour progression and tumour size within each stage. A univariate and multivariate analysis was performed, using surgical waiting time as a categorical variable, to test for associations with disease progression or adverse pathological characteristics.

Results: The median time from first consultation to surgery was 41 days. For the entire group the mean follow-up was 26.6 months. The waiting time stage for stage was: clinical T1 57.12 (SD 49.4) days, clinical T2 36.8 (SD 28.62) days, clinical T3 and T4 30.32 (SD 22.1) days. On multivariate analysis pathological tumour size ($p = 0.0011$) was associated with progression, whereas no significant association was found between waiting time and upstaging ($p = 0.737$). Higher stage tumours ($p = 0.0005$), sarcomatoid pathology ($p = 0.0273$) and clinical evidence of progression ($p = 0.0435$) were associated with shorter waiting times for early interventions.

Conclusion: There was no statistically significant evidence for upstaging or progression during the waiting period for our group of patients. The data suggest that it is safe for the majority of clinical T1 patients to wait 90 days for their surgery. Whether or not other patients with higher clinical stage can be triaged within the same time frame will require prospective study.

POD-5.03

Active surveillance of small renal masses: a prospective multicenter Canadian trial

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Introduction and Objective: The incidence of asymptomatic small renal masses (SRMs) is increasing due to widespread imaging. This trend has led to a stage and grade migration in patients diagnosed with incidental renal cell carcinoma (RCC). To better define the natural history of small renal masses, we are evaluating patients newly diagnosed with SRMs consistent with stage T1a renal cell carcinoma (RCC) managed by active surveillance in a phase II trial.

Materials and Methods: Eight centres across Canada (Renal Cell Carcinoma Consortium of Canada -RC[4]) prospectively enrolled 131 patients with 151 SRMs over 3 years to August 2008. Patients were eligible if elderly had comorbidity and/or refused treatment. Percutaneous needle biopsy was offered for pathological diagnosis, genomic analysis and tissue banking. Serial imaging was performed at baseline, 3, 6, then every 6 months thereafter. Pathologically reported benign tumours were imaged annually. Tumour progression was defined as growth greater than 4 cm or doubling of volume within 12 months. The study end points were rate and time to progression and rate of tumour growth.

Results: The mean tumour diameter at diagnosis was 2.2 (median 2.1, range 0.4–4) cm. Seventy-two biopsies were performed, and confirmed malignancy in 61%, while 13% were benign and 26% nondiagnostic. Mean follow-up was 15 months. Average growth rate did not differ statistically from zero (0.35 mm/yr, $p = 0.08$). Two patients developed metastatic RCC at 5 months (died at 32 mo) and 12 months postenrolment. Seven patients met our criteria for tumour progression but 3 of those continue to be followed due to underlying comorbidities. Seven patients died from unrelated causes. Eighteen patients were withdrawn due to patient or surgeon preference of which 11 went on to treatment and 7 were lost to follow-up.

Conclusion: Early results of our prospective RC[4] active surveillance trial confirms that the majority of SRMs, even if biopsy proven RCC, initially grow at a negligible rate. Initial active surveillance with delayed treatment for progression appears to be a reasonable initial management option in the majority of these patients. The risks of delayed treatment for tumour progression need to be determined with longer follow-up. Notably, 2 SRMs progressed to metastases, suggesting that tumour size is only one prognostic factor, and that additional prognostic markers are needed.

POD-5.04

Assessment of the minimum number of lymph nodes needed to accurately stage renal cell carcinoma at radical nephrectomy

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Introduction and Objective: The goal of the current study was to determine whether a minimum threshold number of nodes exists for detecting one or several positive nodes, thereby accurately staging the pN variable in patients submitted to radical nephrectomy (RN) and lymph node dissection (LND) for renal cell carcinoma (RCC).

Material and Methods: The study included 821 consecutive patients who underwent RN and LND between 1987 and 2006 in 3 urological centres. Median patient age was 60 (range 27–88) years. Lymphadenectomy was perfomed at the discretion of the primary surgeon. Receiver operating curve (ROC) coordinates were used to determine the probability of diagnosing lymph node invasion according to the total number of nodes removed. Additionally, the relationship between the number of nodes removed and the rate of positive lymph nodes was tested in univariable and multivariable logistic regression models.

Results: Of 821 patients, 153 (18.6%) had positive lymph nodes. Patient characteristics: pT1/pT1/pT3a/pT3b/pT3c/pT4: 220/100/249/206/33/13; G1/G2/G3/G4: 51/425/305/40; M0/M+: 627/194. Median number of LNs removed was 9 (range 1–23); median number of positive LNs was 3 (range 1–20). The mean number of lymph nodes removed was 10.2 (median 9, range 1–43). The receiver operating characteristics coordinates plot indicated that the removal of 18 nodes yielded a 90% probability to detect one or several positive lymph nodes. The removal of 12 nodes resulted in a 75% probability of finding one or several positive nodes. A higher number of removed lymph nodes was independently associated with detection of lymph node invasion on multivariable logistic regression analysis adjusted for the effects of the preoperative variables age, tumour dimension, clinical distant metastases and lymphadenopathy ($p = 0.003$; odds ratio 1.04) and for the effects of pathological stage and grade ($p < 0.001$; odds ratio 1.05). These results were confirmed even in the subgroup of patients without distant metastases ($p = 0.04$ and 0.02, respectively).

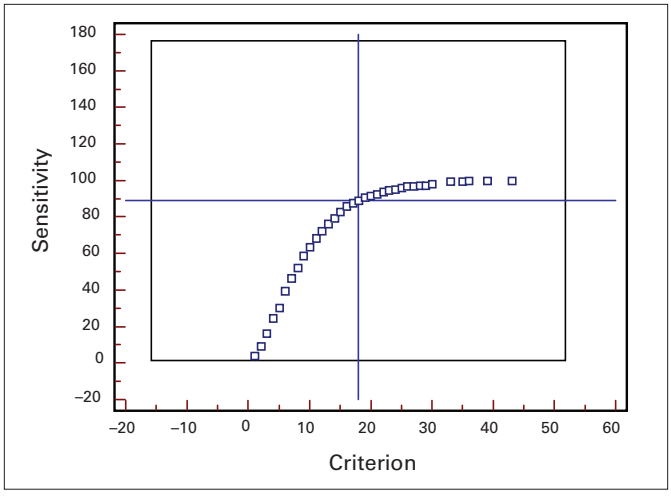

Fig. 1

Conclusion: Our data indicate that at least 12 nodes have to be removed at radical nephrectomy to achieve a 75% probability of finding one or several positive nodes. Further improvement of the specificity of lymphadenectomy will require the removal of a higher number of lymph nodes. The number of removed LNs was significantly associated with the detection of lymph node invasion in our population overall and in the subgroup of patients without distant metastases (Fig. 1).

POD-5.05

A survey of Canadian urologists on current opinion and management of renal cell carcinoma

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Introduction and Objective: Indications for performing partial nephrectomy (PN) in the management of renal cell carcinoma (RCC) are not clearly defined, and the surgery is underutilized despite its proven benefits in preserving renal function. We hypothesize that there exists significant variation in surgical decision-making to performing PN versus radical nephrectomy (RN) for RCC among urologists.

Materials and Methods: From March 2008 to present, a total of 480 surveys were mailed to members of the Canadian Urological Association (CUA). The survey consisted of 3 parts: 1) staff surgeon demographic information; 2) current surgical roster and management of RCC; and 3) preference for performing PN, RN, or either, for a series of 64 case-based scenarios with consideration to tumour size and location, and patient age and comorbidities.

Results: We received a total of 296 surveys (61.7% response rate) from staff urologists. One hundred sixty-four respondents performed both PN and RN in their current practice. Thirty-one respondents (18.9%) were fellowship-trained in urological oncology and 73 (44.5%) worked within an academic hospital setting. One hundred forty-eight respondents (91.4%) had encountered a clinical situation in which there was uncertainty whether to perform PN or RN. Tumour factors (size and location) and patient factors (age and comorbidities) were considered important determinants. Particularly, the decision to perform PN or RN became more unclear in scenarios with smaller tumours (3 cm) abutting the renal collecting system, in the middle-aged patient (50 yr) with comorbid disease.

Conclusion: There are specific scenarios, influenced by both tumour and patient factors, that demonstrate equipoise in performing PN versus RN for RCC. Future clinical trials would be valuable in helping to resolve such clinical dilemmas.

POD-5.06

Laparoscopic nephroureterectomy does not undermine cancer control outcomes in selected patients with nonmetastatic upper tract urothelial carcinoma: a multi-institutional analysis of 1249 cases

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Introduction and Objective: Data regarding the oncological efficacy of laparoscopic nephroureterectomy (LNU) relative to open nephroureterectomy (ONU) are scarce. We used a multi-institutional series of ONU and LNU cases to compare the effect of procedure type (ONU v. LNU) on recurrence and cause-specific mortality rates of upper tract urothelial carcinoma (UTUC).

Materials and Methods: Thirteen centres from 3 continents contributed detailed data on 1249 patients with nonmetastatic upper tract urothelial carcinoma (UTUC). Univariable and multivariable survival models tested the effect of procedure type (ONU, $n = 979$ v. LNU, $n = 270$) on cancer recurrence and mortality rates. Covariates consisted of institution, age, ECOG performance status and tumour characteristics pT stage, pN stage, grade, necrosis, lymphovascular invasion, tumour location, ureteral

management, previous urothelial bladder cancer, architecture, previous endoscopy and concomitant carcinoma in situ.
Results: Median follow-up for censored cases was 49 (mean 62) months. Relative to ONU, patients treated with LNU were older (median age 70 v. 69 yr, $p = 0.01$), had less adverse pathology stage (pT0/Ta/Tis 38.1% v. 20.8%, $p < 0.001$) and more favourable pathological features (papillary architecture 81.9% v. 75.3% $p = 0.02$, presence of lymphovascular invasion 14.8% v. 21.3% $p = 0.02$, presence of necrosis 15.2% v. 23.6% $p = 0.01$). Finally, ureteral tumour location was less likely in LNU versus ONU cases (64.5% v. 71.1%, $p = 0.04$). In univariable models (UVA) addressing cancer-specific mortality, ONU was associated with significantly higher mortality rates ($p = 0.008$). After adjustment for all available confounding variables, in multivariable (MVA) models, the benefit regarding cancer-specific survival related to LNU disappeared ($p = 0.2$). The same results were recorded in the statistical analyses that addressed recurrence risk (UVA $p < 0.001$; MVA $p = 0.2$).
Conclusion: Laparoscopic nephroureterectomy had equivalent oncologic control to ONU in patients with clinically localized UTUC. Laparoscopic approach for the renal portion of nephroureterectomy is a reasonable alternative in the treatment of clinically localized UTUC. However, further studies are needed to compare the morbidity and convalescence time of LNU to that of ONU.