Natural History of Complex Renal Cysts: Clinical Evidence Supporting Active Surveillance

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Purpose: We evaluated intervention rates, progression and cancer specific survival outcomes in patients with complex renal cysts in a single center experience.

Materials and Methods: We used the Montage™ radiology data mining system to retrospectively identify all reported cases of complex renal cyst at our institution from 2001 to 2013. The primary study end points were overall and cancer specific survival. The secondary end points included radiographic progression and upgrading, clinical progression and final histology on surgical pathology.

Results: We identified 336 patients with a complex renal cyst, of whom 185 (55.1%), 122 (36.3%) and 29 (8.6%) had Bosniak IIF, III and IV cysts, respectively. Median followup was 67.1 months (range 34.4 to 101.6). In the 332 patients with followup there was 1 cancer specific death (0.3%) and overall mortality was 6.2%. Ten (5.4%), 37 (30.3%) and 18 patients (62.1%) with Bosniak IIF, III and IV, respectively, underwent surgical or ablative intervention. The indication for intervention was predominantly age (intervention vs no intervention mean ± SD age 50.1 ± 15.9 vs 62.5 ± 13.9 years) and complexity. Surgery with radical and partial nephrectomy (23 patients or 35% and 37 or 57%, respectively) was most common and favorable final pathology was identified. Two treated patients experienced recurrence during followup. When excluding patients with von Hippel-Lindau syndrome, the cancer specific survival rate was 100%.

Conclusions: Cancer survival and overall survival in patients with Bosniak IIF to IV renal cysts was high with only 1 cancer specific death. No cancer deaths were recorded in patients who did not undergo intervention. Reconsidering management guidelines for complex renal cysts is warranted, particularly consideration for initial surveillance of Bosniak III cysts.

Key Words: kidney neoplasms; carcinoma, renal cell; cysts; von Hippel-Lindau disease; mortality

Abbreviations and Acronyms

CSS = cancer specific survival
FG = Fuhrman grade
RCC = renal cell carcinoma
SRM = small renal masses
VHL = von Hippel-Lindau syndrome

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THE incidence of RCC has been steadily increasing by 3% to 4% annually, likely due to greater use of cross-sectional imaging with stage migration toward SRMs.[1–3] In 2016 there were approximately 62,700 new cases of RCC but mortality has not increased by the same amount.[4] With the increasing identification of solid SRMs and RCC there has also been increased identification of cystic renal masses and 8% to 15% of them may have a complex appearance.[5–7]

Since the introduction of the Bosniak classification of renal cysts,[8] the management of renal cysts has been

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primarily guided by radiographic assessment. Based on radiographic features of possible malignancy (septa presence and thickness, calcifications, enhancement, solid components and size) identified on triphasic computerized tomography, cystic renal masses are classified as Bosniak I to IV. Modification of the classification in 1993 introduced the IIF category or Bosniak II cysts with features that warranted short term (3 to 6-month) imaging surveillance.[9–11]

Recent meta-analyses have described a RCC incidence of 6% to 18%, 51% to 55% and 89% to 91% for Bosniak IIF, III and IV cysts, respectively.[11] Based on this correlation guidelines for managing cystic renal masses have typically recommended surgical excision for Bosniak III and IV lesions while close surveillance is recommended for Bosniak IIF lesions.[12,13]

However, more recent population based studies have established that cystic RCC has better CSS than solid clear cell RCC of the same clinical stage, specifically clinical T1b and T2 lesions.[14,15] Smith et al surveyed a small cohort of patients with Bosniak IIF and III cysts, and found that locally advanced or metastatic disease developed in none of them.[14] With no large studies of the natural history of cystic renal masses it is unclear whether these incidentally found cystic renal masses warrant the aggressive surgical treatment that is currently recommended.

As active surveillance has continued to change the management of small solid renal masses, perhaps the time has come to consider surveillance of potentially indolent cystic renal masses. We describe what is to our knowledge the largest institutional series of surveillance for cystic renal masses.

PATIENTS AND METHODS

The research and ethics board approved a retrospective review of all radiology reports at our academic health center, including 2 large urban general hospitals and Princess Margaret Cancer Centre, between 2001 and 2013. The unique Montage™ radiology record crawler system was used to search for the term "complex cyst" in patients who underwent abdominal imaging (computerized tomography, ultrasound or magnetic resonance imaging) for any reason.

Montage is a leading software solution used for health care data mining which enables users to search entire databases using terms of interest. It subsequently generates anonymized reports with accession numbers, which were then used to retrieve patient identifiers in the radiology information system.[16]

Following this identification we reviewed the imaging report and the patient chart to confirm accuracy. After selecting all patients with accurately identified Bosniak IIF, III and IV renal cysts we performed a detailed chart review. Patient demographics (age, gender, proven VHL status, smoking status and comorbidities), cyst characteristics during followup (location, Bosniak classification features and category, and size), imaging modalities (modality, number of scans and radiologist upgrade) and intervention rate (percutaneous biopsy and/or definitive therapy, and pathology findings) were recorded.

Patients were stratified by the initial Bosniak classification. Descriptive statistics were then used to assess these cohorts. We recorded the median and range of continuous variables and used the frequency and proportion to describe categorical variables. Continuous variables were compared by the Mann-Whitney test and categorical variables were compared by the Fisher exact test.

Followup was defined as the time in months between the initial abdominal imaging test with sufficient detail to provide the Bosniak classification to the date of the last clinical assessment, the final scan or patient death.

The primary study end points were CSS and overall survival. The secondary end points were radiographic or clinical progression, the rate of surgical/ablative intervention, radiologist upgrading and final histology on surgical pathology. Radiologist upgrading was defined as formal Bosniak upgrading to a higher classification or subjective worsening of radiographic features in the same Bosniak classification.

All statistical tests were 2-sided with $p < 0.05$ considered significant. The 95% CIs are reported. All analyses were performed with R (https://www.r-project.org/).

RESULTS

Demographics

Of the 336 identified patients 185 (55.1%), 122 (36.3%) and 29 (8.6%) had Bosniak IIF, III and IV cysts, respectively (table 1). Besides having slightly larger cysts at diagnosis and a higher incidence of VHL, patients with Bosniak IV cysts were more likely to undergo biopsy and intervention than patients with Bosniak IIF or III cysts. The 3 cohorts were similar in age and gender. Median followup in the entire cohort was 67.1 months and it was similar among the 3 subsets. In the patients a median of 6 abdominal images (IQR 3–9) were obtained per year.

Active Surveillance Outcomes

Radiologist upgrading was noted during followup in 10 surveillance cases, including 5 upgraded from Bosniak IIF to III (table 2). There were no upgrades from Bosniak III to IV.

Metastatic spread developed in only 1 patient undergoing surveillance. This 89-year-old man was on surveillance for 12 years for an asymptomatic Bosniak IV cyst, which was 2.3 cm at diagnosis. He refused treatment and was followed for 2 years with stable imaging and no evidence of progression.