Active surveillance as the preferred management option for small renal masses

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The changing epidemiology of kidney cancer

Kidney cancer accounts for about 3% of all adult cancers.[1] The incidence of renal cell carcinoma (RCC) in Canada and the United States is increasing at a rate of 2% to 2.5% per year.[1,2] The incidence of RCC in the United States increased from 7.1 per 100 000 in the early 1980s to 10.9 in 2002. Most of this rise is at the expense of incidentally detected small renal masses (SRMs) likely due to the more frequent use of abdominal imaging. In 1970, 10% of RCCs were detected incidentally, compared with more than 60% in 1998. These incidentally detected SRMs portend a better prognosis than symptomatic ones. Patard and colleagues described that the 73 months disease-free survival for incidentally detected tumours was 93% compared with 59% for those that presented with symptoms.

These incidentally detected SRMs are more likely to be of benign histology, smaller, of lower stage and lower grade.[3] Cooperberg and colleagues demonstrated that the mean tumour size at diagnosis decreased from 4.1 to 3.6 cm between 1993 and 2004.[4] The resected tumour size from surgical series dropped from an average largest diameter of 7.8 to 5.3 cm between 1989 and 1998.[5] There has also been an increase in the proportion of renal masses ≤3 cm and ≤2 cm between 1993 and 2004 (32.5 vs. 43.4% and 24.1 vs. 29.4%, respectively). In addition, it has been described that 85% of tumours ≤4 cm in size were localized to the kidney (stage T1a) as opposed to 32% of those between 4 and 7 cm. Pearson and colleagues reported that only 7.2% of tumours ≤4 cm are stage pT3a.[6] From a sample size of 18 818 patients, Rothman and colleagues reported that 86% of patient with tumours smaller than 4cm in diameter have a low Fuhrman grade.[7]

Patients in the seventh to ninth decades of life have experienced the largest increase in incidence with a tenfold rise between 1935-39 and 1985-89.[2] This particular age group has the largest amount of comorbidities. It has been demonstrated that the 5-year overall mortality for no cancer causes and other cancers is much higher than that of kidney cancer in patients older than 65 years of age.[8]

While disease characteristics have changed over the last 30 years, aggressive treatment remains the standard of care for incidentally detected SRMs. Between 1983 and 2002, the incidence of renal surgery in the United States increased from 0.9 to 3.6 per 100 000, mostly at the expense of SRMs. This increase in surgical treatment does not appear to translate into better outcomes. The mortality rate for all renal tumours in the United States has increased.[2,9] Furthermore, Russo and colleagues demonstrated that progression-free survival and overall survival rates have not changed between 1989 and 2004 after resection of localized kidney cancer.[10] These changing trends demonstrate a treatment disconnect between the stage migration of RCC and increased surgical management and the rising disease specific mortality rate of RCC. This observation questions the risk that these incidentally detected SRMs truly represents.

The nature of small renal masses

Most solid renal masses are RCCs. Several studies have demonstrated that chromophobe and papillary carcinomas have a better prognosis than clear cell type carcinomas. In addition, patients who present with papillary and chromophobe RCCs tend to have tumours of lower stage compared with patients who have clear cell RCC.[11]

Historical series reported that about 90% of solid renal masses were RCCs. Although the sensitivity and specificity for renal cortical tumours have been reported to be as high as 100% and 95% respectively, the specificity and diagnostic accuracy of computerized tomography for SRMs decreased.[12] Several more recent reports have shown that for SRMs the proportion of benign histology after partial or radical nephrectomy can be up to 46%.[11] It has also been demonstrated that elderly patients with SRMs are up to 3.5 times more likely to have benign lesions than RCC.

Several preoperative predictors of benign versus malignant disease have been identified. Traditionally, tumour size has been reported as the best predictor. We have recently demonstrated that in this era of smaller, incidentally detected renal masses, tumour location has replaced tumour size as a predictor of benign disease.[13] We hypothesized that

prediction of benign versus malignant disease may be as important as prediction of prognosis in the presence of a renal malignancy.

It is unique to the management of renal masses to embark upon complex surgical procedures, such as partial and radical nephrectomies without prior tissue diagnosis, particularly when the proportion of benign disease in SRMs is high. Biopsies of renal masses have traditionally not been performed due to the perceived high risk of tract tumour seeding and hemorrhagic complications. Careful scrutiny of the literature demonstrates that tumour seeding has been reported in only 5 cases despite the thousands of biopsies performed worldwide. Complications, including hemorrhage, do not appear to be significant with present biopsy techniques.[14] Masses smaller than 1 cm can be biopsied, although biopsies of masses greater than 2 cm are more likely to provide useful information. A high degree of accuracy can be achieved with respect to tissue sampling interpretation, which can report sensitivity and specificity has high as 100%, and accuracy ranging from 70% to 90%.[14,15] The use of percutaneous biopsies can have a significant effect on decision-making and cost. Wood and colleagues demonstrated a 44% change in the treatment plan based on biopsy results.[16] Although the use of percutaneous renal biopsies in the management of localized RCC promises novel ways to define preoperative tumour markers and markers of disease progression through the combination of histologic and molecular or cytogenetic techniques, outside of the research realm, they infrequently affect upon management decisions.

The natural history of small renal masses

Several centres have reported their series of patients with renal masses that were followed with active surveillance. Chawla and colleagues published their meta-analysis in which they analyzed 234 lesions from 9 different centres.[17] They demonstrated that the average growth rate for these masses was 0.28 cm per year. Of those masses where histological information was available (46%), 92% were RCC. Progression to metastatic disease was observed in three patients (1% of the lesions). Importantly, all 3 patients presented with symptoms at diagnosis and therefore, did not have an incidentally detected renal mass. Following this meta-analysis, several centres have published their own series and other centres have updated their results. All these publications continue to show a slow growth rate and a low risk of progression to metastatic disease.

Crispen and colleagues reported their series of 82 patients in whom management was delayed for a median of 14 months.[18] They demonstrated that most lesions (62%) did not show an interval growth and that treatment options were not altered in a single patient due to changes in the radiographic appearance of their tumour during the period of delay. Furthermore, they demonstrated that an initial period of surveillance did not limit eventual treatment options or outcomes.

This review of the currently available literature on the natural history of untreated renal masses provides valuable insight into why the detection of these indolent lesions has not led yet to a demonstrable decrease in mortality from this disease.

Treatment alternatives

The current standard of care of SRMs is partial nephrectomy. Excellent cancer control rates have been achieved after surgical excision of these lesions. Large series reporting outcomes of open and laparoscopic partial nephrectomy performed by highly skilled surgeons at large-volume centres have described complication rates of 20%.[19] These and other series demonstrate that in the most experienced surgical hands partial nephrectomy has a significant risk of hemorrhage and urologic and non-urologic complications, as well as a significant risk of subsequent surgical interventions. Although these complications pose an acceptable risk in the young and healthy patient, they may outweigh the benefits when treating older or infirm patients.

The reality of an aging population favours a cautious approach to detecting disease and managing medical problems. It has been demonstrated that the potential benefit for even completely effective therapies decreases with age.[20] The combination of a higher burden of competing risks in the aging population, the non-aggressive natural history of most SRMs and the significant rates of treatment-related risks conspires to reduce the net benefit of the surgical management of SRMs.

Conclusion

These data do not suggest that RCC is not lethal and that RCC is not surgical. Instead, these data suggest that not all SRMs are lethal, that they do not all grow, that progression to metastatic disease is rare and that we appear to be overestimating the treatment effect of surgery. Based on this evidence, there may be a role for a period of initial active surveillance as part of the management of incidentally detected SRMs followed by treatment only for those that show progression. These findings appear to be in line with the trend observed in the management of early stage prostate cancer with overtreatment of potentially insignificant disease.

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