

CHANGING PRACTICE IN THE MANAGEMENT OF SMALL RENAL MASS

Small renal masses are defined as solid renal tumors that enhance on computed tomography (CT) and magnetic resonance imaging (MRI) and are suspected of being renal cell carcinomas (RCC). They are generally low-stage and relatively small (< 4 cm in diameter) at presentation. Recently throughout the world, as well as in Bangladesh, management of small renal mass has been changing. This is not only due to increasing diagnosis, but also for their varied biological behaviors, interpretation of various imaging modalities, tissue sampling and varied treatment options.

We do not have any statistics in Bangladesh. However in the United States in the year 2010, as estimated 58,000 new cases of RCC were diagnosed¹. The rate is increasing by 3% to 4% per year as the use of CT and MRI increases^{2,3}. On the other hand we see stage migration in renal tumour diagnosis, i.e. more tumours are now being discovered in clinical stage T1⁴. Currently, clinical T1 renal tumors account for 48% to 66% of cases⁵. The clinical presentation of RCC has also changed. Previously, systemic manifestations or paraneoplastic syndromes such as hypercalcemia or hypertension were more common in patients with metastatic renal cell carcinoma, so they were called internist tumour. Now most are discovered incidentally on CT or MRI done for various abdominal symptoms, so they termed now as radiologist tumour.

Small renal masses vary in biologic aggressiveness. Despite early diagnosis and treatment, mortality from RCC has not been declined. This Suggest that many of these small renal mass does not require aggressive surgical treatment⁶. Data from larger series indicates that 20% of small renal masses are benign, such as oncocytoma, atypical or fat-poor angiomyolipoma, metanephric adenoma, urothelial carcinoma, metastatic lesions, lymphoma, renal abscess, renal infarction, mixed epithelial or stromal tumor, pseudotumor, and vascular malformations. Fifty five percent to 60% of small renal mass are indolent renal cell carcinomas and 20% to 25% have potentially aggressive features, defined by high nuclear grade or locally invasive characteristics^{7,8,9}.

Predictor of aggressiveness for small renal mass has been defined by some observer. Size directly correlates with the risk of malignant pathology. When tumours are less the < 1.0 cm, 38% to 46% are benign, and when > 7.0 cm, 6.3% to 7.1% are benign. But Size at presentation did not predict the growth rate⁷. 1.0-cm increase in tumor diameter correlates with a 16% increase in the risk of malignancy¹⁰. There have been no documented reports of disease progression in the absence of demonstrable tumor growth¹¹. Type 2 papillary RCCs, mostly high grade and have worse prognosis compared with type 1 papillary RCCs. Chromophobe RCCs found to have better prognosis compared with papillary and clear cell RCCs¹².

Ultrasound is the most commonly used diagnostic technique and may be used in subsequent surveillance without radiation burden. Ultrasound has particular utility in the characterization of cystic masses, including hyperdense cysts that may pose a diagnostic challenge to CT. The sensitivity of ultrasound decreases with tumor size. At 1 cm, ultrasound was only able to identify 20% of masses, compared with 76% identified by CT. The detection rate becomes equal when the lesions measured 3.5 cm¹³. Contrast-enhanced ultrasound with intravascular microbubble contrast agents can assess enhancement of vascular elements within tissue and a detection specificity of 96.4% and a sensitivity of 77.3%^{14,15}. Triple-phase CT is ideal, >15 Hounsfield units (HU) of enhancement on CT imaging are considered suggestive of RCC, < 10 HU of enhancement are more likely to be benign. Enhancement in the range of 10 to 15 HU is considered equivocal¹⁶. In CT scan angiomyolipoma merits a special attention. With rare exceptions, dense fat within a renal mass reliably indicates benign angiomyolipoma. Beyond this, no clinical or radiological feature ensures that a small renal mass is benign. MRI normally done when patient allergic to IV contrast or have moderate renal dysfunction.

Renal mass sampling has been done with percutaneous needle biopsy or cytology. These were not routinely performed previously due to over 18% false-negative

rates and potential morbidity¹⁷. A negative biopsy could not be trusted and renal mass sampling would not ultimately change patient management. Needle biopsy traditionally had a restricted role to diagnose renal lymphoma, carcinoma that had metastasized to the kidney and primary renal abscess. After 2001 renal mass sampling has become safer and more accurate than thought. A meta-analysis of contemporary series indicate that its accuracy in differentiating benign from malignant tumors is actually greater than 95%¹⁸. In addition, false-negative rates are now consistently less than 1%. When biopsy results are noninformative (10% cases) then biopsy can be repeated, or the mass can be surgically excised, or the patient can undergo conservative management if he or she is unfit or unwilling to undergo surgery. Serious complications requiring clinical intervention or hospitalization occur in less than 1% of cases. The risk of tumor seeding is now estimated to be less than 0.01%¹⁸. Recent studies have also indicated that molecular profiling through gene expression analysis or proteomic analysis can further improve the accuracy of renal mass sampling¹⁹.

Radical Nephrectomy, partial nephrectomy, minimal invasive surgery, thermal ablation therapy and active surveillance all has been tried for small renal mass from time to time. The reference standard treatment of RCC is radical nephrectomy as defined by Robson et al. In 1969²⁰. The cancer-specific survival rate for pT1a tumors is 97%²¹. However when technically feasible, partial nephrectomy gives equal oncologic outcome for T1 lesions. Partial nephrectomy is more technically difficult as it involves renal reconstruction but conserves renal tissue. Radical nephrectomy is now indicated for technically unfavorable lesions because of their location and comorbidity²². Over the last decade, various studies have highlighted the association between radical nephrectomy and the subsequent clinical onset of chronic kidney disease, and cardiovascular events and elevated mortality rates²³. The situation is quite different in renal transplant, where donors undergo stringent screening to ensure that their general health is good and that their renal function is robust, both of which are not true in many patients with small renal masses, particularly if they are elderly. The overuse of radical nephrectomy prompted the AUA to commission a panel to provide guidelines for the management of clinical stage T1 renal masses. After an extensive review and rigorous meta-analysis, the panel concluded that partial nephrectomy is the gold standard for most

patients²³. Complication rates for partial nephrectomy are slightly greater than those for radical nephrectomy. Laparoscopic partial nephrectomy is a highly challenging surgical procedure that demands specialized laparoscopic training²⁴. There appear to be equivalent functional and early oncologic outcomes²⁴. Robot assisted laparoscopic partial nephrectomy is making the thing easier but at increasing cost.

Thermal Ablation therapy with radiofrequency ablation and cryoablation has been used in selected cases. They can be used with percutaneous, open or laparoscopic approach. Radiofrequency ablation (RFA) using a needle probe with temperatures up to 105°C causes cell death and coagulation necrosis²⁵. 5-year actuarial metastasis-free and cancer-specific survival rates is around 95% and 99%, respectively²⁶. However, there are concerns about the use of radiologic criteria for the assessment of tumor viability. Cryoablation, introduced in 1995 decreases tissue temperature to -40°C, destroying the tumor by cellular damage resulting from freezing, apoptosis, coagulation necrosis, and immunologic action²⁷. Experience is limited for ablation of renal masses with high-intensity focused ultrasound. There is also no standard protocol recommendation for frequency of follow-up imaging after the ablation²⁸. The majority of local recurrences after ablation have been successfully retreated by subsequent ablation²⁹.

Active surveillance involves careful initial monitoring for progression, with treatment delayed. The new term small renal mass has become increasingly relevant for today's urological practice. Many small renal masses are benign. Active surveillance is a relatively new approach for the treatment of renal tumors and is particularly indicated for elderly and infirm patients. It is recommended to biopsy before making a treatment decision in the event that the tumor is benign. Cross-sectional imaging of the abdomen with CT scan is usually performed at 3, 6, and 12 months; then every 6 months for 2 years and yearly thereafter^{30,31}. Ultrasound or MRI is acceptable for patients with contraindications to CT. Chest radiography are performed annually to detect asymptomatic metastasis.

So, management for small renal mass has changed. An initial CT-or ultrasound-guided percutaneous biopsy should be considered for any patient with a newly diagnosed small renal mass. The treatment decision should be made after assessment of age, comorbidities, tumor characteristics (i.e., location and size), imaging characteristics, and histologic diagnosis, if available. In

this scenario, I emphasize to develop the skill of our histopathology diagnosis. Where possible, partial nephrectomy should be considered as gold standard for removing small renal mass. Radical nephrectomy should be considered for technically unfavorable lesions because of their location and comorbidity. It should not be done for only cosmetic reason using laparoscope or robot assistance, as chance of chronic kidney disease is high after radical nephrectomy. Thermal Ablation Therapy with Radio frequency ablation and Ablation can be used in selected cases. Active surveillance is a treatment option for many patients, particularly elderly and infirm patients.

Small renal masses are a distinct entity, and the clinical approach should be different from those previously established for renal cell carcinomas.

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Abbreviations:

- RCC : Renal cell carcinoma
 CT : Computed tomography