Canadian Guidelines for Management of the Small Renal Mass (SRM)


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DEFINITION OF SMALL RENAL MASS (SRM)

SRMs as a clinical entity are defined as enhancing tumours <4cm in diameter with image characteristics consistent with stage T1aN0M0 RCC[1-5]. Most, but not all, SRMs are renal cell carcinoma (RCC). Assessment must exclude metastases in which case the patient would be considered to have metastatic RCC with a small primary tumour (T1aN0M+).

INTRODUCTION

The incidence of SRMs has increased with the widespread use of imaging and this, in turn, has increased the incidence of RCC. Mortality rates are not increasing despite the rising incidence and increased treatment[6, 7]. The established standard treatment for localized RCC has been radical nephrectomy[8]. More recently, partial nephrectomy has become the recommended treatment[9,
Results of surgical therapy are excellent, with >90% disease specific survival for stage T1a[11]. Probe ablation and active surveillance are alternative management strategies with similar efficacy[12].

SRMs are frequent in the elderly and infirm, in whom the risk of treatment must be weighed against life expectancy and malignant potential of the tumour [5]. Approximately 20-25% of SRMs are benign[13]. Even if proven malignant, most SRMs grow slowly. Most studies have reported that the rates of malignant vs. benign pathology, higher grade, higher pathological stage, growth and the risk of metastasis increases with tumour size. Small RCCs may be associated with metastatic disease at diagnosis in up to 8% of cases, so initial staging of all SRM patients is essential[14]. Based on current data, initial Active Surveillance (AS) with delayed treatment for local progression appears to be a relatively safe initial management strategy.

METHODS
A literature review of the electronic Medline database was performed. Citations from included articles and review articles were manually searched by the chair, Dr. Michael Jewett, and a draft guideline developed. The draft guideline was reviewed by the guideline writing committee. Suggestions were encorporated and the final draft was approved by the same committee and submitted to the CUA guideline committee for subsequent approval and promulgation in 2014. It is anticipated that this guideline will be reviewed and updated at regular intervals.

ROLE OF NEEDLE CORE BIOPSY OF SRMs
The Kidney Cancer Research Network of Canada (KCRNC) Consensus following the January 2013 Canadian Kidney Cancer Forum describes needle biopsy for histologic characterization as an option that may guide treatment decisions and that should be reserved for patients in whom the results might change management. Biopsy should be done at the time of probe ablation, if not
before[9,15]. There is Canadian experience with needle core biopsy of SRMs[13,16]. Biopsy appears safe and at least 80% of first biopsies are diagnostic. Repeat biopsy may be considered. The frequent benign pathology found with excised SRMs and the lack of specificity in imaging has lead to increasing acceptance of a role for pretreatment biopsy[5,17]. Successful biopsy requires expertise in interventional imaging and pathology[12]. Multiple tumours may have different histology and tumour grade, so multiple and repeat biopsies may be required to accurately characterize tumour histology. However, biopsy is not yet a standard of care in Canada.

MANAGEMENT OPTIONS FOR SRMs

The Canadian Consensus for the management of early stage T1a RCC states the following options[15,18):

- Partial nephrectomy (PN) is recommended – by open, laparoscopic or robot assisted laparoscopic means.
- Laparoscopic radical nephrectomy (RN) is reserved for tumours not amenable to partial nephrectomy
- Probe ablation by radiofrequency (RFA) or cryotherapy. A biopsy should be obtained before or at the time of ablation.
- Active surveillance (AS)

PARTIAL NEPHRECTOMY

There is increasing concern about the use of nephrectomy, as opposed to nephron-sparing surgery or partial nephrectomy (PN), for localized kidney cancer. While it has been considered the gold standard treatment for RCC, it is becoming clearer that partial nephrectomy is associated with a lower risk of long term renal dysfunction and reduces overtreatment of benign tumours[19-22].

The only level I evidence regarding oncological outcomes of PN compared to RN is controversial and has been discussed in the Canadian Consensus[15,23-26]. The EORTC trial was underpowered and closed prematurely due to poor enrollment, despite a prolonged accrual. It is still generally believed that PN is not inferior to RN. Laparoscopic partial nephrectomy is increasingly
available in Canada and experience with robot-assisted laparoscopic partial nephrectomy is growing in Canada.[27-28] Controversy continues to surround the role of intraoperative cooling remains controversial as well as the optimal method and time limit for renal ischemia. It is generally accepted that minimizing warm ischemia is prudent, but we await the results of ongoing clinical trials. Open partial nephrectomy is preferable to laparoscopic nephrectomy. Partial nephrectomy can result in complications including bleeding, a need for transfusion, urinary fistula and acute changes in renal function. There is no consensus regarding the optimal surveillance after PN but the CUA guideline, “Follow up guidelines after radical or partial nephrectomy”, should be followed [15,29].

THERMAL OR PROBE ABLATION – RADIOFREQUENCY ABLATION (RFA), CRYOTHEAPY

Percutaneous probe ablation is becoming more widely accepted and practiced but it is important to have a biopsy before or at the time of treatment for follow-up planning and outcome analysis[30]. Morbidity is low and ablation can be performed on an outpatient basis without general anesthesia in a cost effective manner. It is an attractive approach in elderly and infirm patients. Long-term followup with imaging is required and local recurrence occurs in up to 14% of patients[3]. The definition of ablative success remains controversial, as many tumours were not biopsied pretreatment. Complications are relatively uncommon and well described including transient pain, and damage to adjacent organs and the collecting system. Renal function appears to be well preserved. Tumour location is the most important aspect of patient selection, with reduced success rates for endophytic central tumours. Laparoscopic approaches are unnecessary. Anterior tumours are approached laparoscopically in some centres, but partial nephrectomy should be considered if operative exposure is undertaken. Success rates decrease in tumours larger than 3 cm in diameter. Reports with longer term follow-up of sizeable numbers of patients demonstrate good oncological efficacy in carefully selected patients and repeat treatments are possible[31,32]. Salvage surgery is technically difficult and usually requires nephrectomy. The clinical significance of reported outcomes is frequently weakened by the lack of biopsy and rate of retreatment.
The number of centres offering ablation is limited and most centres focus on one method. Cryotherapy can be monitored during treatment by using ultrasound to visualize the ice ball although experienced RF ablators can see changes in the tumour and use impedance or temperature for monitoring.

**ACTIVE SURVEILLANCE (AS)**

All AS studies of SRMs have relatively short followup but low rates of progression, including a low rate of metastasis of 1-2%. Most are not biopsy proven to be cancer. Long-term followup is required to establish the safety of this approach in the young and fit patient. Prognostic factors for progression are poorly understood but primary tumour growth rate is the most widely used trigger for delayed treatment[33].

AS with regular radiographic follow-up should be a primary consideration for SRMs in elderly and/or infirm patients with multiple comorbidities that would make them high risk for intervention, and in those with limited life expectancy [25,28].

For follow-up during the surveillance period, Rendon et al suggested CT or MRI every 3 months in the first year, every 6 months in the next two years and every year thereafter [23]. This high number of CT scans was considered necessary to assure a safe surveillance strategy. However, in this regard, the recognized risk of radiation exposure due to multiple CT scans should be kept in mind. The optimum protocol and imaging modality is unknown at present, but ultrasound, with or without contrast, may provide adequate images for measurement.

**SUMMARY**

Needle core biopsy is increasingly performed, but is not yet the standard of care for histological characterization of SRMs. Partial nephrectomy (PN) is recommended for SRMs. Pure and/or robot assisted laparoscopic PN is an option in experienced centres. Laparoscopic radical nephrectomy is recommended for those tumours not amenable to PN. Probe ablation is an alternative
treatment, but biopsy should be obtained before or at the time of ablation to guide followup. Experience with active surveillance is currently limited by short followup, but should be a primary consideration in the elderly and infirm.

REFERENCES

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