
Canadian Urological Association guidelines for followup of patients after treatment of non-metastatic renal cell carcinoma

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Originally published in *Can Urol Assoc J* 2018;12(8):231-8.
<http://dx.doi.org/10.5489/cuaj.5462>



Disclosures

Dr. Kassouf: Received grants/honoraria from Astellas, AstraZeneca, Janssen, Merck, and Roche

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Dr. Kapoor: Advisor for and participant in clinical trials supported by Amgen, Astellas, GSK, Janssen, Novartis, Pfizer, and Sanofi.

Dr. Lattouf: Advisor for AbbVie, Amgen, Astellas, Novartis, and Pfizer; received an educational grant from Janssen

Dr. Leveridge: Advisor for Astellas

Dr. Power: Participant in clinical trial supported by Argos Therapeutics

Dr. Pouliot: Advisor for, Amgen, Astellas, and Pfizer; speaker for Sanofi; received payment/grants/honoraria from Amgen, Astellas, Astra Zeneca, Janssen, Pfizer, and Sanofi

Dr. So: Speaker for Amgen, Astellas, and Janssen.

Dr. Tanguay: Advisor for Pfizer; received travel grants from Sanofi



Renal cell carcinoma

- 3% of all malignancies
- Risk factors
 - Smoking, obesity, hypertension
 - ACKD, occupational exposure
 - Hereditary (VHL, HPRC, HLRCC, BHD, SHD-RCC, TSC)
- Surgical resection (radical or partial nx) remains most common treatment
- Ablation increasingly used



Methods

- Publications on surveillance after surgery are based on retrospective analysis, including some larger, multicentre studies and well-designed controlled studies
- Randomized prospective studies are sparse, rendering it difficult to obtain qualified evidence-based data
- No clear consensus on surveillance after surgical extirpation for patients with RCC
- Followup approach based on assessment of timing and location of RCC recurrence in a risk-stratified manner



Rationale for surveillance

- Surveillance after surgery monitors for
 - Postoperative complications
 - Renal function
 - Local recurrence
 - Recurrence in the contralateral kidney
 - Development of metastasis



Rationale for surveillance cont'd

- Renal function and postoperative complications are commonly assessed by:
 - Hx & PE; eGFR and Hgb at 4–6 weeks
- Long-term monitoring of renal function
 - Long-term monitoring of serum eGFR, and proteinuria is recommended in patients with compromised renal function prior to surgery or significant decrease in eGFR after surgery
 - Referral to a nephrologist if eGFR <45 ml/min/1.73m² or progressive CKD develops after surgery, especially if associated with proteinuria (Grade B)



Rationale for surveillance cont'd

- Recurrence in the ipsilateral kidney is associated with positive surgical margins, multifocality, higher stage and grade
- Tumours may develop in the contralateral kidney (incidence <2%)
- Early diagnosis of local and contralateral kidney recurrence is useful since majority can be cured with treatment (LOE 3)



Rationale for surveillance cont'd

- Extensive tumour recurrence reduces the possibility of complete surgical resection
- Patients who underwent surgery when local recurrences became symptomatic have a higher rate of incomplete resection, positive surgical margins, and worse survival
- Early diagnosis of disease relapse may enhance efficacy of systemic therapy or allow for metastatectomy if the tumour burden is low (LOE 4; Grade C)

Kapoor, CUAJ 2017; Psutka, BJUI 2017; Levy, J Urol 1998

Hence, support rationale for surveillance to detect recurrences and metastases early (LOE 4; Grade C)



Prognostic factors

- Anatomical
 - Local extent of the primary tumor (LOE 3)
 - Presence of nodal metastasis (LOE 3)
- Histological
 - RCC subtypes (LOE 3)
 - Carcomatoid dedifferentiation
 - Tumour grade (LOE 4)
 - Other tumour characteristics (size, histological coagulative necrosis, DNA ploidy) (LOE 4)
- Clinical
 - ECOG status (LOE 3)
 - Presence of symptoms (local and systemic)
 - Serum blood parameters (LOE 4)
- Molecular
 - Carbonic anhydrase IX, VEGF, HIF
 - Ki67, p53, PTEN, E-cadherins, PD-L1, others
 - Not recommended in clinical setting (Grade C)

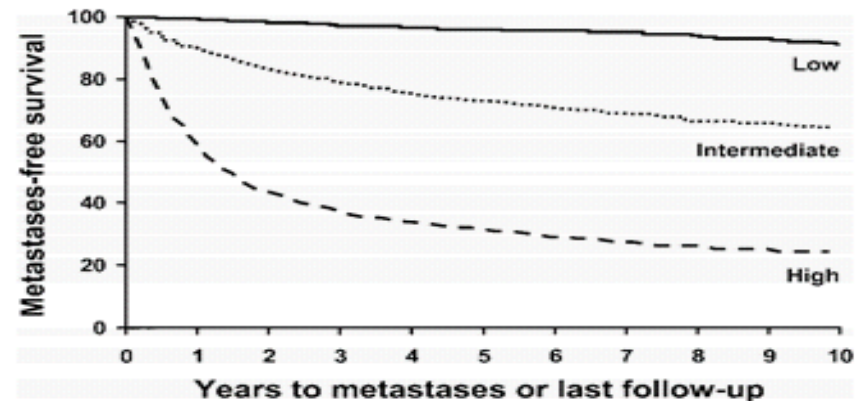
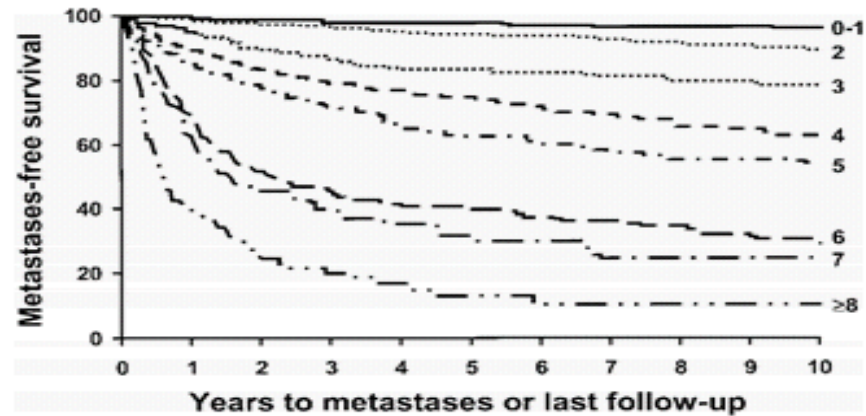


Predictive models

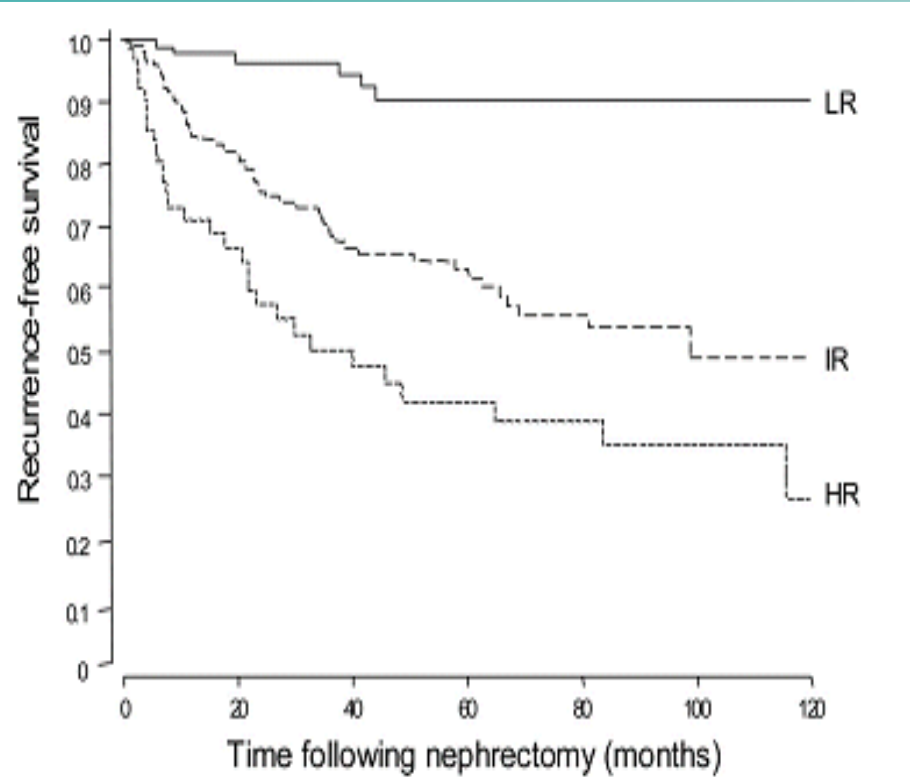
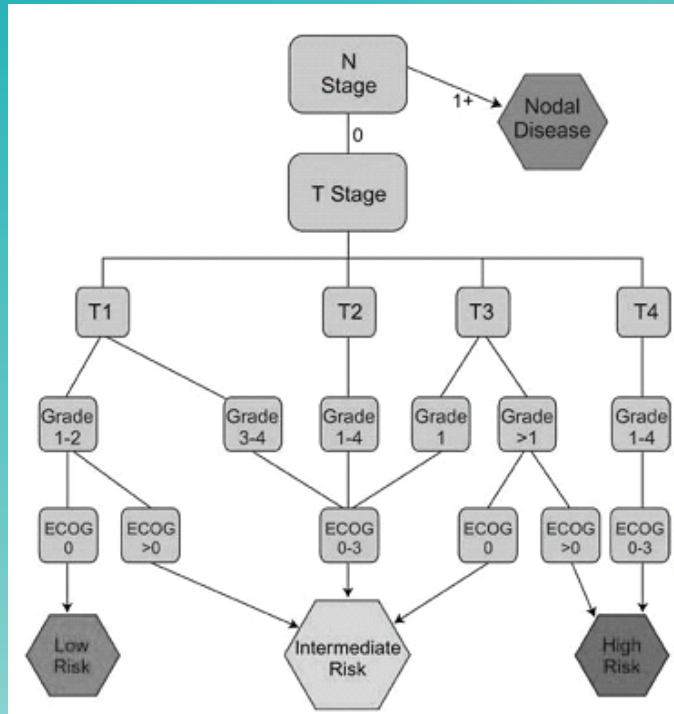
Scoring Algorithm to Predict Metastases after Radical Nephrectomy in Patients with Clear Cell Renal Cell Carcinoma

Feature	Score
Primary tumor status (pathologic T stage) ^a	
pT 1a	0
pT 1b	2
pT 2	3
pT 3a	4
pT 3b	4
pT 3c	4
pT 4	4
Regional lymph node status (N stage) ^a	
pNx	0
pN0	0
pN1	2
pN2	2
Tumor size (cm)	
< 10	0
≥ 10	1
Nuclear grade	
1	0
2	0
3	1
4	3
Histologic tumor necrosis	
No	0
Yes	1

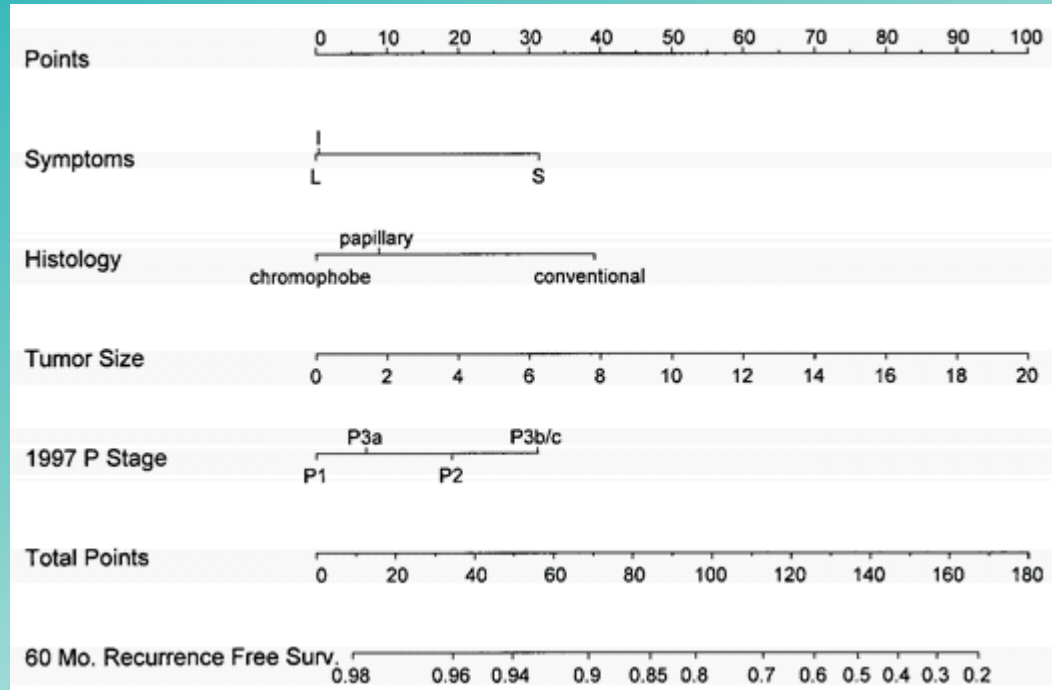
^a According to the 2002 American Joint Committee on Cancer TNM staging system.¹⁹



Predictive models cont'd



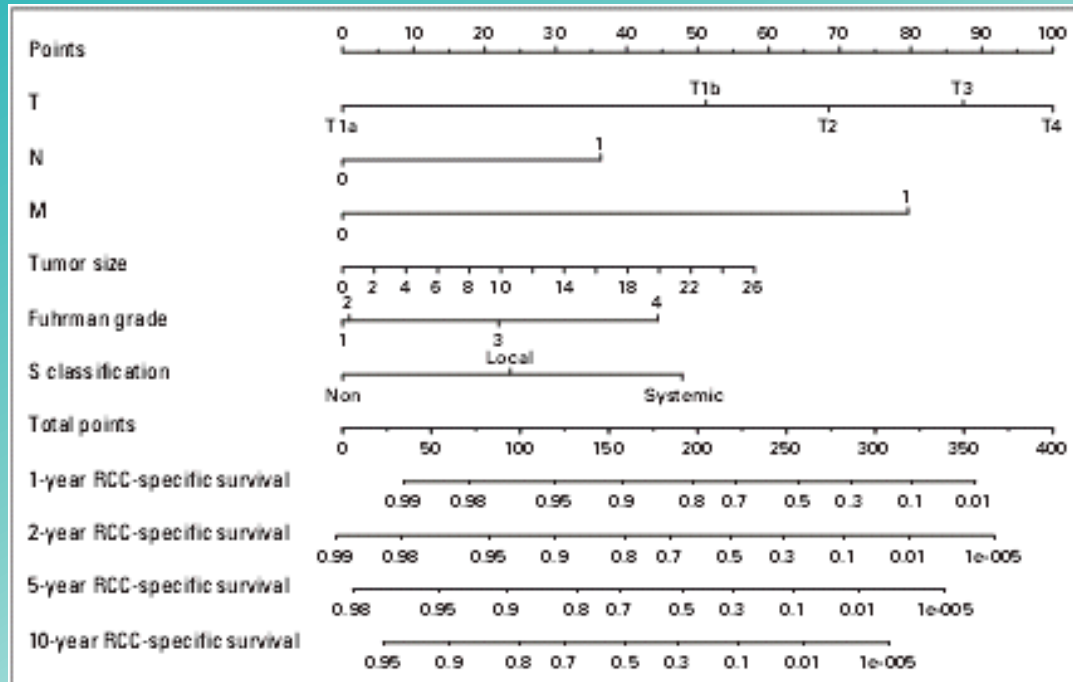
Predictive models cont'd



Kattan, J Urol 2001



Predictive models cont'd



Predictive models cont'd

- Several prognostic models have been published and externally validated
- Have not been proven superior over the stage-adapted followup
- Integrated prognostic system or nomograms not routinely recommended for followup



CUA guidelines

- Canadian guidelines will be based on pathological stage
- Other prognostic factors have not been integrated to more or less stringent f/u protocol (Grade C)



CUA guidelines cont'd

- In absence of randomized studies, conclusions based on large nonrandomized cohorts with long-term followup
- Pulmonary recurrences
 - Routine chest x-ray is recommended. In higher risk patients, CT chest may be performed due to the higher sensitivity (LOE 5; Grade D)
- Abdominal recurrences
 - CT abdomen/pelvis is recommended, particularly in cases of tumor-associated symptoms; an abdominal ultrasound may be performed for lower risk patients (pT1-2) (LOE 4; Grade C)



CUA guidelines cont'd

- CT head or bone scan is not routinely recommended unless clinically indicated (LOE 4; Grade C)
- PET-CT is not recommended for surveillance in RCC



pT1

- Levy, *J Urol* 1998
 - Recurrence rate: 7% (median followup 39 months)
 - Median time to recurrence: 38 months (range 18–67)
 - Majority of recurrences were in lung; no recurrences in abdomen
 - None of the pulmonary recurrences were symptomatic.
- Stephenson, *J Urol* 2004 (Canadian group)
 - Recurrence rate: 5.3% (median followup 44 months)
 - Median time to recurrence: 35 months (range 2–93)
 - Only 0.9% of patients recurred at 13, 66, and 93 months in the renal fossa and were asymptomatic



T1

- Local recurrences \approx 2%
- Local recurrences more common for larger tumours following PN and ablated tumours



pT1

- Overall 7% develop recurrences; median time to recurrence 35–38 months
 - Half will occur after 5 years
 - 5% for T1a and 15% for T1b
- Late recurrence rates:
 - T1a: 2.6% T1b: 5%
 - T2a: 9% T2b: 10%
 - T3a: 11% T3b: 22%



pT1 cont'd

- Most common location of 1st recurrence:
 - Lung (54%), lymph nodes (22%)
 - Bone (20%), and liver (15%)
- Independent predictors of late recurrence:
 - Lymphovascular invasion
 - Furhman grade 3 or 4
 - Pathological tumour stage >pT1



Recommended surveillance for T1

- Clinical assessment, blood biochemistry, and chest x-ray every year (LOE 4; Grade C)
- Abdominal CT, MRI or US is recommended at 24 and 60 months (LOE 4; Grade C)
- Routine imaging beyond 5 years is optional and can be risk-adapted (Grade D)
- Followup is the same for partial nephrectomy for <4 cm lesions (LOE 2; Grade B)
- Since local recurrence rates in this population is similar to radical nephrectomy
- CT abdomen at 3–12 months postop for patients treated with partial nephrectomy is optional (LOE 4; Grade C)



Recommended surveillance: Ablated T1a tumours

- Similar to surgically treated tumours except for
 - Abdominal imaging (CT or MRI) at 3, 6, and 12 months, then annually thereafter for up to 5 years (LOE 4; Grade C)
- If pre-treatment biopsy demonstrated benign tumor and imaging post ablation shows treatment success, routine imaging beyond one year is not recommended (LOE 5; Grade D)



pT2

- Several series have reported recurrences rates 25–35% after a median followup of 5 years
- Levy, *J Urol* 1998
 - Recurrence rate: 27% at a median followup of 53 months
 - Median time to recurrence: 32 months (range 3–115)
 - Only 2 patients developed metastasis within 6 months postop
- Stephenson, *J Urol* 2004 (Canadian group)
 - Recurrence rate: 17% at a median followup of 38 months (asymptomatic 50%)
 - Median time to recurrence: 25 months (range 3–95)



Recommended surveillance for T2

- Clinical assessment, blood biochemistry, and CXR (or chest CT) every 6 months for 3 years then yearly (LOE 4; Grade C)
- Abdominal CT/MRI/US recommended at 12, 24, 36, 60 months (LOE 4; Grade C)
- Routine imaging beyond 5 years is at the discretion of the treating physician



pT3-4

- MDACC, *J Urol* 1998
 - Recurrence rate: 39% at a median followup of 31 months
 - Median time to recurrence: 17 months (range 2–88)
- Stephenson, *J Urol* 2004 (Canadian group)
 - Recurrence rate: 34%; asymptomatic: 40%
 - Median time to relapse: 14 months for pT3a; 9 months for pT3b
- Dabestani, *World J Urol*, 2016
 - Recurrence rate at 5-year followup: 42–47%
 - Median time to recurrence: 21 months



Recommended surveillance for T3-4

- Clinical assessment, blood biochemistry, and CXR (or chest CT) every 6 months for 3 years then yearly (LOE 4; Grade C)
- Abdominal CT or MRI recommended at 6, 12, 18, 24, 36 months, then every 2 years (LOE 4; Grade C)
- In pN+ disease,
 - CXR (or chest CT) and abdominal CT/MRI are recommended at 3 and 6 months, then every 6 months for 3 years then yearly (LOE 4; Grade C)



EAU 2017

Risk profile	Surveillance						
	6 mo	1 y	2 y	3 y	4 y	5 y	> 5 y
Low	US	CT	US	CT	US	CT	Discharge
Intermediate	CT	CT	CT	US	CT	CT	CT once every 2 years
High	CT	CT	CT	CT	CT	CT	CT once every 2 years

ESMO 2016

The follow-up scheme for localised RCC following surgery should depend on the therapeutic possibilities upon recurrence. CT scans of thorax and abdomen are routinely carried out, with time intervals depending on risk factors. It is recommended to perform CT scans every 3–6 months in high-risk patients for the first 2 years, while a yearly CT scan is probably sufficient in low-risk patients (expert opinion).

Long-term follow-up is proposed in some institutions, due to the possibility of late relapse, but its benefit has never been demonstrated.



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FOLLOW-UP^{a,b} (category 2B)

Stage I (pT1a) and (pT1b)^c

Follow-up After a Partial or Radical Nephrectomy

- H&P every 6 mo for 2 y, then annually up to 5 y after nephrectomy
- Comprehensive metabolic panel and other tests as indicated every 6 mo for 2 y, then annually up to 5 y after nephrectomy
- Abdominal imaging:
 - ▶ After partial nephrectomy:
 - ◊ Baseline abdominal CT, MRI, or US within 3–12 mo of surgery
 - ◊ If the initial postoperative scan is negative, abdominal CT, MRI, or US may be considered annually for 3 y based on individual risk factors
 - ▶ After radical nephrectomy:
 - ◊ Patients should undergo abdominal CT, MRI, or US within 3–12 mo of surgery
 - ◊ If the initial postoperative imaging is negative, abdominal imaging beyond 12 mo may be performed at the discretion of the physician
- Chest imaging: Chest x-ray or CT annually for 3 y, then as clinically indicated
- Pelvic CT or MRI, as clinically indicated
- CT or MRI of head or MRI of spine, as clinically indicated
- Bone scan, as clinically indicated



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FOLLOW-UP^{a,b} (category 2B)

Stage II or III

Follow-up After a Radical Nephrectomy^c

- H&P every 3–6 mo for 3 y, then annually up to 5 y after radical nephrectomy and then as clinically indicated thereafter
- Comprehensive metabolic panel and other tests as indicated every 6 mo for 2 y, then annually up to 5 y after radical nephrectomy, then as clinically indicated thereafter
- Abdominal imaging:
 - › Baseline abdominal CT or MRI within 3–6 mo, then CT, MRI, or US (US is category 2B for Stage III), every 3–6 mo for at least 3 y and then annually up to 5 y
 - › Imaging beyond 5 y: as clinically indicated
 - › Site-specific imaging: as symptoms warrant
- Chest imaging:
 - › Baseline chest CT within 3–6 mo after radical nephrectomy with continued imaging (CT or chest x-ray) every 3–6 mo for at least 3 y and then annually up to 5 y
 - › Imaging beyond 5 y: as clinically indicated based on individual patient characteristics and tumor risk factors
- Pelvic CT or MRI, as clinically indicated
- CT or MRI of head or MRI of spine, as clinically indicated



AUA 2013

T1

T2-4 or N+

Follow-Up Measure	Low Risk	Moderate to High Risk
Abdominal Scan ¹ /Imaging ²	<p>Partial Nephrectomy—Obtain a baseline abdominal scan¹ (CT or MRI) within three to twelve months following surgery;</p> <ul style="list-style-type: none"> If the initial postoperative scan is negative, abdominal imaging² (US, CT OR MRI) may be performed yearly for three years based on individual risk factors <p>Radical Nephrectomy—Patients should undergo abdominal imaging² (US, CT or MRI) within three to twelve months following renal surgery;</p> <ul style="list-style-type: none"> If the initial postoperative imaging is negative, abdominal imaging² beyond twelve months may be performed at the discretion of the clinician 	<p>A baseline abdominal scan¹ (CT or MRI) within three to six months following surgery with continued imaging² (US, CT or MRI) every six months for at least three years and annually thereafter to year five.</p> <ul style="list-style-type: none"> Imaging² beyond five years may be performed at the discretion of the clinician. Perform site specific imaging as symptoms warrant.
Chest Imaging/scan	<ul style="list-style-type: none"> Obtain a yearly chest x-ray for three years and only as clinically indicated beyond that time period 	<ul style="list-style-type: none"> Obtain a baseline chest scan (CT) within three to six months following surgery with continued imaging³ (CXR or CT) every six months for at least three years and annually thereafter to year five. Imaging³ beyond five years is optional and should be based on individual patient characteristics and tumor risk factors

CUA 2018

Months Post-op	3	6	12	18	24	30	36	48	60
Low Risk (pT1)									
Hx & PE			x		x		x	x	x
Blood test			x		x		x	x	x
CXR			x		x		x	x	x
Abdominal CT/MRI/US					x				x
Intermediate Risk (pT2)									
Hx & PE		x	x	x	x	x	x	x	x
Blood test		x	x	x	x	x	x	x	x
CXR or Chest CT		x	x	x	x	x	x	x	x
Abdominal CT/MRI/US			x		x		x		x
High Risk (pT3-4)									
Hx & PE		x	x	x	x	x	x	x	x
Blood test		x	x	x	x	x	x	x	x
CXR or Chest CT		x	x	x	x	x	x	x	x
Abdominal CT/MRI		x	x	x	x		x		x
Very High Risk (pTxN+)									
Hx & PE	x	x	x	x	x	x	x	x	x
Blood test	x	x	x	x	x	x	x	x	x
CXR or Chest CT	x	x	x	x	x	x	x	x	x
Abdominal CT/MRI	x	x	x	x	x	x	x	x	x



Followup post-ablation for T1a

Months after surgery

	3	6	12	18	24	30	36	48	60
cT1a									
H&P			X		X		X	X	X
Blds			X		X		X	X	X
CXR			X		X		X	X	X
CT/MR	X	X	X		X		X	X	X

