# Follow-up imaging after nephrectomy for cancer in Canada: urologists' compliance with guidelines and cost of surveillance

Alice Dragomir, PhD<sup>1</sup>, Noémie Prévost<sup>1</sup> MSc, Armen Aprikian, MD<sup>1</sup>, Anil Kapoor, MD<sup>2</sup>, Antonio Finelli, MD<sup>3</sup>, Frédéric Pouliot, MD<sup>4</sup>, Ricardo Rendon, MD<sup>5</sup>, Peter C. Black, MD<sup>6</sup>, Ronald Moore, MD<sup>7</sup>, Rodney H. Breau, MD<sup>8</sup>, Jun Kawakami, MD<sup>9</sup>, Darrell Drachenberg, MD<sup>10</sup>, Jean Baptiste Lattouf, MD<sup>11</sup>, and Simon Tanguay, MD<sup>1</sup>

<sup>1</sup>McGill University and McGill University Health Center, Montreal, Qué; <sup>2</sup>McMaster University, Hamilton, Ont.; <sup>3</sup>Princess Margaret Cancer Centre and University of Toronto, Toronto, Ont.; <sup>4</sup>Université Laval, Quebec City; <sup>5</sup>Dalhousie University and Queen Elizabeth II Health Sciences Centre, Halifax, Nov.; <sup>6</sup>University of British Columbia, Vancouver, Bri.; <sup>7</sup>University of Alberta, Edmonton, Alb.; <sup>8</sup>University of Ottawa, Ottawa, Ont.; <sup>9</sup>University of Alberta, Calgary, Alb.; <sup>10</sup>University of Manitoba, Winnipeg, Man.; <sup>11</sup>University of Montreal, Montreal, Qué.

#### Competing interests: None declared

#### Funding:

Supported in part by the Cote-Sharp Program in Health Economics at McGill University Health Center

**Key words:** imaging surveillance, nephrectomy for cancer, urologists' compliance with guidelines **Words count:** 3,521

#### **Correspondence to:**

Alice Dragomir Ph.D Assistant Professor, Urology/Surgery, McGill University Scientist health economics and outcomes research Research Institute of the McGill University Health Center Alice.dragomir@muhc.mcgill.ca

#### Background

Surgical tumor removal remains the preferred treatment option for most patients with renal cell carcinoma. Many medical associations have proposed guidelines for the optimal surveillance of patients following surgery. The goal of our study was to evaluate the adherence of Canadian urologists to the follow-up guidelines proposed by the Canadian Urological Association (CUA) and the economic impact of surveillance in Canada.

#### Methods

The cohort studied was identified from the Canadian Kidney Cancer information system (CKCis) which is prospectively populated database. Patients included in this cohort underwent radical or partial nephrectomy for a pT1-3N0M0 renal cancer between January 2011 and June 2016. Abdominal and thoracic imaging performed during the follow-up period was captured and compared with the CUA guidelines.

#### Results

A total of 1,982 patients from 15 academic institutions were identified. Of the 1,982 patients, 1,380 were pT1, 164 were pT2 and 438 were pT3. Post operatively, 1,948 chest imaging and 2,986 abdominal imaging studies were performed. There was incongruent adherence to the CUA post-operative surveillance guideline with an observed to recommended ratio of 0.71 and 2.27 for chest and abdominal imaging respectively. The highest disparity in chest imaging was observed in pT2 patients (0.54) and the highest disparity in abdominal imaging in pT1 patients (4.55). The sub-optimal adherence to follow-up guidelines costs approximately \$50 millions dollars over a period of 5 years in Canada.

#### Conclusion

In Canada, there are large differences in imaging surveillance between guidelines and clinical practice. Adherence to guidelines could result in significant cost savings.

#### Introduction

According to the Canadian Cancer Statistics, 6,200 Canadians were diagnosed with kidney cancer in 2015(1). The rise in renal cell carcinoma (RCC) diagnoses has been partly attributed to the widespread use of medical imaging and the incidental findings of renal tumours on computed tomography (CT) and ultrasound (US) (2, 3). In Canada, the age-standardized incidence rate of kidney cancer has increased by 1.3% per year for men and by 1.1% per year for women between 2001 and 2010(1).

Surgical resection, either via radical or partial nephrectomy, is the most effective therapeutic option for clinically localized RCC. While radical nephrectomy has long been considered the gold standard (4), partial nephrectomy (PN), or nephron-sparing surgery, has now replaced it as the treatment of choice for renal masses of up to 7 cm (5). PN has been shown to reduce overall mortality and non-cancer–related death rates (6-9). Moreover, PN allows for kidney function preservation (10) and reduces the need for dialysis and transplantation (11, 12). Recurrence rates of 0%–6% are similar between PN and radical nephrectomy for small tumours (12-15).

Radiologic follow-up after partial or radical nephrectomy aims to identify local recurrence or development of metastatic disease. The most common sites of metastatic recurrence are the lung, liver, bone, and brain (16). Although high-level evidence is lacking, it is hypothesized that early diagnosis of recurrence or metastasis could trigger earlier treatment and thus improve patient outcomes (5).

Urological associations have proposed different algorithms for follow-up after partial or radical nephrectomy (5, 17, 18). The Canadian Urological Association (CUA) has approved guidelines for the follow-up of patients with localized and locally advanced RCC after partial or radical nephrectomy (18, 19).

Despite the publication of these guidelines, recent studies have shown that adoption and adherence to guidelines by the clinical community remain suboptimal (20, 21). Despite the overall underutilization of post-nephrectomy imaging, concerns regarding possible overuse in patients at low risk for recurrence and underuse in those at greater risk have been suggested. New surveillance imaging guidelines may reduce unwarranted variability and promote risk-based, cost-effective post-nephrectomy management.

Due to the expensive nature of imaging studies, the overall cost of patient surveillance after partial or radical nephrectomy is expected to be important. A previous study suggests that imaging surveillance capturing 95% of all recurrences would cost between \$10,000 to \$13,000 per patient, depending on the type of nephrectomy (radical or partial) and the risk group (22).

To date, little is known about urologists' compliance with published guidelines in Canada and the cost associated with current surveillance trends. This study aims to evaluate the levels of compliance with the guidelines, factors associated with the compliance, and their economic impact in the real-life Canadian setting by using a prospective cohort of patients undergoing partial or radical nephrectomy in several academic centers in Canada.

#### Methods

Data sources

The cohort study was identified from the Canadian Kidney Cancer information system (CKCis). Initiated in January 2011, CKCis is a multicentre collaboration of 15 academic hospitals in six Canadian provinces. Clinical, demographic, and pathological data are obtained by patient survey and medical record review.

Patient characteristics collected in CKCis included age, gender, body mass index (BMI), preoperative renal function (estimated glomerular filtration rate [eGFR]), smoking history, hypertension, diabetes, cardiovascular disease, and family history. Tumour characteristics included stage, size, and number of renal tumours. Treatment characteristics included year of surgery, type of surgery (partial or radical nephrectomy), and surgical approach (open, laparoscopic or robotic assisted).

#### Study cohort

Patients included in this study were diagnosed with renal cell carcinoma between January 2011 and June 2016. Patients with no previous history of kidney cancer and undergoing treatment after January 2011 in the participating centers across Canada were identified. Several exclusion criteria were applied, as indicated in Figure 1. Patients were stratified by pathological tumour stage in three stage groups based on post-surgery pathological findings using the 2009 TNM staging system (23). All patients in our cohort had N0 and M0 status, therefore stages pT1N0M0, pT2N0M0, and pT3N0M0 will be referred as pT1, pT2, and pT3, respectively. The surveillance period (follow-up period) was defined from the date of the nephrectomy until the end of follow-up, which corresponds either to the date of disease recurrence or date of last follow-up (i.e., last patient visit to the treating physician). Recurrence was defined as detection of metastasis in the chest or abdomen as evidenced by imaging (computed tomography [CT], ultrasound [US], or X-ray [XR]).

#### Chest and abdominal imaging tests for surveillance after nephrectomy

The number of chest and abdominal imaging tests performed for each patient was captured in CKCis during the follow-up period. The CUA guidelines were used to estimate the recommended number of chest and abdominal imaging tests for each patient during the specific follow-up period (Figure 2). Any imaging tests performed during the first 28 postoperative days, as well as repeated tests were excluded from this calculation. A test was considered to be a repetition if the same test was identified at the same location within the previous 30 days.

#### Statistical analysis

Patient characteristics were presented as percentages, means (95% confidence interval [CI]) and medians (interquartile range [IQR]) as applicable. The Kaplan-Meier method was used to estimate the freedom from recurrence stratified by tumor stage.

Three levels of compliance were defined: 1) compliant-testing (number of observed equal to number recommended); 2) under-testing (number of observed less than the number recommended) and 3) over-testing (number of observed more than the number recommended).

To measure the level of compliance between the observed surveillance imaging tests and the recommended as per the Canadian guidelines, weighted Kappa statistics and Pearson and Spearman correlation statistics were applied overall and by stage group. Pearson and Spearman correlation statistics tested whether the number of observed chest and abdominal imaging tests was in agreement with the respective recommended number of tests, while Kappa statistics assessed the consistency between compliance levels in chest surveillance and abdominal surveillance. Levels of

compliance were measured over the entire follow-up period and at different time points (over a 6-, 12-, 18-, and 24-month period).

Multivariate logistic regression was used to evaluate factors associated with noncompliance of chest and abdominal imaging tests (either over-testing or under-testing) in the post-nephrectomy surveillance period.

All analyses were performed using the Statistical Analysis System Software (version 9; SAS Institute, Cary, North Carolina). All tests were two-sided with a significance threshold of 5%.

Several covariates were considered as potential predictors of noncompliance, such as age groups (more than 75 years old vs. less or equal to 75 years old), family history of kidney cancer, smoking status at diagnosis, and type of surgery (radical vs. partial). Tumour characteristics, obtained from the pathology report associated with the procedure, include tumour stage (pT2, pT3, vs. pT1), tumour grade (high v. low), surgical margin status (positive vs. negative), and histology. High grade was defined as Fuhrman grade 3 or 4, and low grade as Fuhrman grade 1 or 2. The lower-risk histology category included papillary and chromophobe RCC. Also, several comorbidities have been evaluated, such as other cancer, diabetes, hypertension, obesity, hypothyroidism, heart disease, kidney stone, renal disease, osteoarthritis, gout, gastroesophageal reflux disease, depression, and chronic pulmonary disease.

#### Economic analysis

Unit median and mean costs of imaging tests were obtained using unit costs from four provinces (Alberta, British Colombia, Quebec, Ontario and Nova Scotia) (24-30). The expected and observed costs of surveillance over the follow-up were calculated both for the overall cohort and by stage group. The economic impact of noncompliance with the surveillance guidelines corresponds to the difference between the expected cost of surveillance and the observed cost of surveillance, for chest and abdominal imaging.

To estimate the overall costs of surveillance and the costs of noncompliance with guidelines at the Canadian level over a comparable surveillance period, the corresponding values from our cohort were extrapolated to the Canadian population susceptible to undergo partial or radical nephrectomy for RCC over the same period (between 2011 and 2015)(1). This estimate was based on the assumptions that the stage group distribution (pT1, pT2, and pT3), the ratio of CXR vs CT chest and the ratio of abdominal CT vs US, the rates of surveillance imaging testing observed from our cohort are generalizable to the national level, and that 75% of Canadian incident kidney cancer cases are T1-T3N0M0 RCC at diagnosis (3, 5, 31, 32).

The estimated cost over a 72-month period, which amounts to the maximum post-nephrectomy surveillance period, was based on the total number of chest and abdominal imaging tests recommended according to the guidelines over this period. The actual expected costs were calculated by extrapolating compliance levels and test modality distributions (CT vs US) observed from our cohort, over the remaining period of up to 72 months; these were evaluated for both our cohort and at the Canadian level.

#### Results

Patient characteristics

2 3 The study cohort included 1,982 subjects with pT1-T3N0M0 RCC treated with either partial or radical nephrectomy. Patient characteristics are presented in Table 1. Of those, 1,380 (70%) were pT1, 164 (8.3%) were pT2, and 438 (22.1%) were pT3. The mean age of patients was 60 years old, and 66% of the patients were men. Nearly half of the nephrectomies were radical (43%), and the majority of patients had clear cell RCC (71.3%). In addition, 10.5% were smokers, 14.7% had complications related to the nephrectomy procedure, and 5.6% had a family history of renal tumors. The most common comorbidities were hypertension (47.9%), dyslipidemia (19.1%), heart disease (19.0%), and diabetes (17.6%). No major differences have been observed in terms of comorbidities distribution between stage groups (data not showed).

The mean length of postoperative surveillance was 18.6 months (range 1-63) and the median was 15 months (IQR 7-28). Recurrence rates in the pT1, pT2, and pT3 groups were 1.9%, 14.6%, and 28.6% at 1 year, and 3.7%, 24.1%, and 39.3% at 2 years.

#### *Compliance with the CUA guidelines*

Table 2 presents the surveillance parameters: aggregated and on a patient-level basis. Over this period of follow up, 1,948 chest and 2,986 abdominal imaging tests were performed. The corresponding estimated recommended tests were: 2,754 and 1,317, respectively. Overall, the ratio of recommended versus observed was 0.71 and 2.27 for chest and abdominal imaging testing, respectively. The highest disparity for chest imaging was observed in pT2 patients (0.54) and for abdominal testing in pT1 patients (4.55). This corresponds with a compliance level of only 42.9%for chest and 35.5% for abdominal imaging testing, with 37.3% of patients receiving fewer chest imaging tests than recommended and 55.3% receiving more abdominal imaging tests than recommended.

When stratified by stage group, approximately 57% of pT2 and 43% of pT3 patients received fewer chest imaging testing than recommended, and 64% of pT1 and 59% of pT2 received more abdominal imaging testing than recommended. We noted that while 67.6% of all recommended tests were chest examinations, only 39.5% of observed tests were for the chest. Furthermore, 56.1% of performed chest examinations were chest X-rays (CXR), and 43.0% of abdominal examinations were US.

Table 3 presents compliance levels at the 6-, 12-, 18-, and 24-month periods. Only minor changes over time were observed in both chest and abdominal imaging.

Kappa statistics indicated very low consistency in compliance levels between chest and abdominal imaging testing, with an overall estimate of 0.30 (95% CI 0.27-0.32). The highest level of agreement was observed in the pT3 group (0.59, 95% CI 0.52–0.66).

The mean and median recommended and observed imaging testing, as well as the Pearson and Spearman correlation coefficients between these measurements are presented in Table 4. Again, low-to-moderate correlations were observed, with the highest value found for recommended and observed abdominal imaging testing in the T3 group (r=0.71, 95% CI 0.66–0.76).

#### Factors associated with conformity to the CUA guidelines

The multivariate logistic regression evaluating factors associated with the probability of having received under-testing revealed several associations, presented in Table 5. Patients having undergone radical nephrectomy and presenting with a higher grade had a lower probability of being under-tested for chest imaging by 39% (odds ratio [OR] 0.61, 95% CI 0.45-0.82) and 33% (OR

No factors associated with the probability of having received abdominal imaging over-testing were found with multivariate logistic regression. A trend toward an increase in the number of abdominal tests in patients with positive margins was observed (OR 1.61, 95% CI 0.98–2.64). However, the probability of receiving abdominal over-testing was reduced by 77% in the pT3 group compared with the pT1 group.

### Economic analysis

The estimated mean and median unit costs are presented in Table 6. Table 7 summarizes the results of the cost of noncompliance with the Canadian clinical guidelines in our cohort. The observed costs of chest and abdominal imaging over the mean surveillance period of 18 months were \$647,110 and \$1,481,035, respectively. The corresponding expected values were \$911,699 and \$688,875, respectively.

The results extrapolated to the Canadian level over the same time period are presented in Table 7. Between 2011 and 2015, we estimated that 31,000 Canadians were diagnosed with kidney cancer, and 23,250 of them were T1-T3N0M0 RCC (70% pT1, 9% pT2, and 21% pT3). For a similar mean follow-up of 18 months, the estimated excess cost attributable to noncompliance with the clinical guidelines for the surveillance of these patients was \$6.2M. This represents an excess amount of \$9.3M for the over-testing of the abdomen and a reduction of \$3.1M attributable to the undertesting of the chest. Specifically, patients in the pT1 group experienced the highest excess cost of abdominal imaging (\$8.7M), while pT3 patients had the lowest cost of surveillance with a difference of -\$1.4M and -\$458,569 between observed and recommended chest and abdominal imaging testing, respectively.

Over a 72-month surveillance period, a total of 160,404 and 68,429 chest and abdominal imaging tests, respectively, should have been performed as per the Canadian guidelines. Based on the compliance level observed over the 18-month period, the actual expected costs in our cohort of 1,982 patients was estimated at \$3.0M for abdominal and \$4.5M for chest imaging (Table 7). This represents an excess abdominal imaging cost of \$4.8M and a reduction of chest imaging cost of \$1.2M. The corresponding values at the Canadian level were estimated at \$57.8M and -\$15.2M, respectively (Table 7).

## Interpretation

This is the first study evaluating Canadian compliance with surveillance guidelines and cost of follow-up after surgery of patients treated for clinically localized RCC. This study reveals a suboptimal level of guideline compliance and a significant cost associated with the overuse of abdominal imaging.

Overall, the agreement between the number of tests performed and number of tests recommended was low. Only half of the patients received chest and abdominal imaging consistent with guideline recommendations. The results revealed under-compliance of chest imaging of 29.3%, and a concomitant potential overuse of abdominal testing of 226.7%, with the highest discrepancy

observed in lower-stage patients (pT1 and pT2). The highest level of noncompliance was observed in pT1 patients, where the number of abdominal testing was 4 times higher than recommended.

Our study found several factors associated with suboptimal surveillance. Specifically, patients having undergone radical nephrectomy, or presenting with a higher stage of disease were associated with decreased risk of being under-tested for chest imaging, while patients in stage pT2 or pT3, and those with conventional clear cell or low-risk histology had an increased risk of under-testing for chest imaging. Yet, higher grade of disease was associated with reduced over-testing, potentially explained by the fact that a higher frequency of abdominal imaging for patients with higher grade is recommended by the guidelines, compared with lower-grade groups.

The estimated cost of noncompliance with the Canadian clinical guidelines in our cohort was important. Overall, the cost associated with chest imaging over the 18-month follow-up period was 27% lower than the expected cost, while the cost of abdominal imaging was more than twice as high as the expected cost. At the Canadian level, over a similar mean follow-up of 18 months, the estimated excess cost attributable to noncompliance with the clinical guidelines for the surveillance of these patients was \$6.1M, with the highest excess cost observed in the pT1 group (approximatively \$8.6M). If the same trend is maintained over the full 72-month period of recommended surveillance, the excess cost associated with noncompliance with the clinical guidelines will be significant (more than \$50M at a Canadian level).

Finally, for both chest and abdominal imaging, no patterns or preferences of usage of imaging modality (i.e., XR and US are less expensive modalities compared with CT), or changes over time were seen during the surveillance period. Regarding the type of imaging, this is probably due to the choice of imaging modality not being clearly defined in the guidelines. To evaluate recurrence in the lung, chest radiography is recommended, with the option to perform CT instead. However, there is insufficient evidence to suggest a benefit in this setting, as no evidence from randomized clinical trials is available; yet the difference in cost of chest CT and chest XR is considerable. To evaluate abdominal recurrences, abdominal CT is recommended, with the option to perform US instead for lower-risk patients (pT1-2N0) (18). In addition, due to lower local recurrence rates in this population, lower-intensity surveillance is generally suggested for abdominal imaging compared with chest imaging, regardless of the initial staging. The indefinite nature of these recommendations reflects the absence of consensus on the subject, which is also observed in the guidelines of the American Urological Association (AUA) and the European Association of Urology (EAU). In a public health care system such as the Canadian system, optimal utilization of health care resources involves the prioritization of less expensive modalities if high-level evidence on the effectiveness of more-costly alternatives is lacking. This study highlighted the high excess cost associated with abdominal over-testing, which is not justified by the available evidence, yet, under-testing in the chest may be associated with lower rates of detection of distant metastasis, and consequently with worse clinical outcomes. In addition, our results showed that clinicians may not be paying attention to the recommended frequency of specific imaging testing based by stage group, and that is why the over-testing is more prominent in the low-stage groups. On the other hand, our study may suggest that there is a discrepancy in recurrence patterns between the guideline recommendations and what urologists actually encounter in their clinical practice. In any case, our study can open this discussion and create awareness about the important economic implications. Further studies are needed to evaluate the impact of noncompliance with the recommended surveillance guidelines and their impact on clinical outcomes.

Two other studies have evaluated post-nephrectomy surveillance imaging; however, without a cost analysis. One recent study revealed the suboptimal post-nephrectomy surveillance of patients treated from 1991 to 2007 (20). For patients followed for at least one year, initial abdominal and chest imaging tests were performed in 69% and 78% of patients, respectively; with yearly rates of abdominal and chest imaging decreasing by year 5 to 28% and 39% in high-risk–disease patients (T3 or T4), and to 21% and 25% in low- to moderate-risk–disease patients (pT1 or pT2). A second study on nephrectomy-treated patients between 2000 to 2009 (21) confirmed these results, by claiming rates of chest and abdominal imaging of 65%–80% and 58%–76%, respectively. While our study confirms these results for chest imaging, it showed an over-usage of abdominal imaging. This might be explained by differences in the time period, which covers contemporary clinical practice in our study, compared with the two aforementioned studies, which evaluated earlier time periods. Additionally, these studies were performed in the American population, and so, this difference may be also related to the difference between the Canadian and American health care systems.

Our study presents some limitations. First, all the patients included in the cohort were followed in academic institutions, therefore results may not be generalizable to surveillance patterns in non-academic institutions. Second, we could not discount the possibility that over-usage of abdominal imaging was due to onset of new symptoms as opposed to routine screening for recurrence, due to the absence of information on why the images were performed. Third, we could not exclude the fact that the cause of noncompliance might reflect the urologists' disagreement with the surveillance guidelines due to lack of strong evidence. However, this would not explain the discrepancy between abdominal and chest imaging tests.

#### Conclusion

This is the first Canadian study evaluating surveillance imaging performed after partial or radical nephrectomy, and the associated costs in the contemporary era. This study revealed suboptimal follow-up surveillance imaging patterns and noncompliance with the recent clinical guidelines. The estimated economic impact was shown to be important, with millions of dollars that can be saved by better adherence to these guidelines. Additional efforts should be made to raise awareness among urologists about appropriate follow-up imaging in this setting.

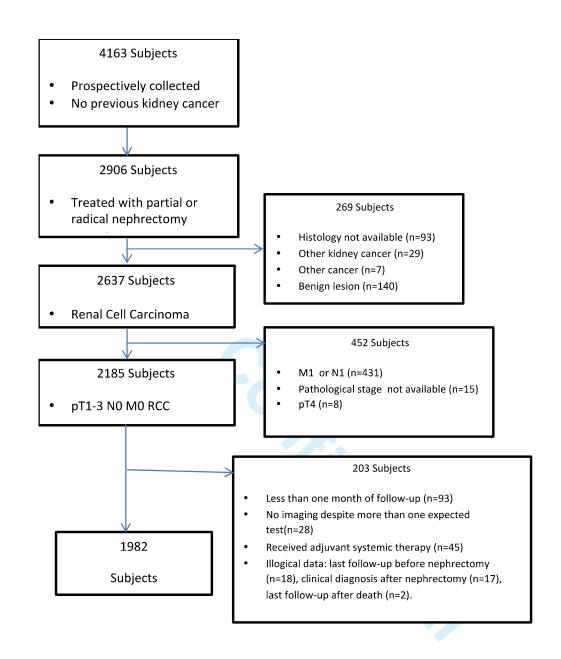


Figure 1: Flow chart of the cohort selection

		Figure 1. Months Post-op								
	3	6	12	18	24	30	36	48	60	72
pT1										
Hx & PE			x		×		х	×	X	Х
Blood test			x		x		х	X	X	X
CXR			x		х		х	X	X	X
CT or U/S abd					х				x	
pT2										
Hx & PE		х	х	х	х	х	X	X	X	X
Blood test		х	x	х	x	х	х	X	x	X
CXR		х	х	х	х	х	х	X	X	X
CT or U/S abd			×				x		x	
pT3										
Hx & PE		х	X	х	х	х	х	X	X	Х
Blood test		x	x	X	x	X	x	x	X	X
CXR		x	x	X	x	х	x	x	x	X
CT abd		х	x	х	х		x		x	
pTxN+										
Hx & PE	х	х	х	х	X	x	x	X	X	X
Blood test	x	x	x	X	x	x	x	x	x	X
CXR	x	x	x	x	x	x	х	X	X	X
CT abd	x	x	x	x	X	x	x	X	X	x

Blood test: include complete blood count, serum chemistries, and liver function tests

CXR: can be alternated with chest CT

CT abd: can be alternated with abdominal ultrasound in pT1-2N0 patients

\* -if patient is symptomatic or abnormal blood test, earlier radiologic investigations may be indicated

-follow-up beyond 72 months, refer to text for more details

Figure 2: CUA follow-up guidelines after radical or partial nephrectomy for localized and locally advanced RCC<sup>16</sup> 

	All Subjects	T1	T2	Т3
Characteristic	<i>n</i> = 1,982	<i>n</i> = 1,380	<i>n</i> = 164	<i>n</i> = 438
Age <sup>*</sup>	60.3	59.5	58.4	63.2
Mean (95% CI)	(59.7–60.8)	(58.9–60.1)	(58.9–60.4)	(62.1–64
Median (IQR)	60.7	60.2	59.4	63.1
	(52.5–68.4)	(52.0–68.0)	(49.5–67.5)	(55.8–71.
Age > 75 yr <sup>*</sup> , %	10.0	8.4	10.4	15.1
Male, %	66.3	64.0	68.3	72.8
High grade <sup>†</sup> , % ( $n = 1,830$ )	43.7	33.2	51.7	72.7
Radical nephrectomy, %	42.7	25.8	85.4	80.1
Positive Surgical margin, $(n = 1,935)$	6.5	4.7	0.6	14.6
Histology‡				
Clear cell RCC, %	71.3	68.8	59.2	84.0
Papillary RCC, %	16.4	18.4	21.3	8.0
Chromophobe RCC, %	7.8	8.3	14.6	3.7
RCC unspecified, %	4.5	4.5	4.8	4.3
CT imaging§, %	52.9	46.4	57.9	71.7
Complications <sup>II</sup> , %	14.7	14.1	15.2	16.4
Family history of RCC, %	5.6	5.7	4.3	5.7
Vital status¶ ( $n = 1,639$ )				
AWD, %	8.1	4.9	12.3	16.6
No evidence of disease %	83.5	88.9	77.9	68.4
Overall death, %	4.1	1.6	8.0	10.6
Lost to FU, %	4.1	4.4	1.8	3.9
Unknown, %	0.20	0.15	0.00	0.46

Note: AWD = alive with disease; CI = confidence interval; CT = computed tomography; FU = follow-up; IQR = interquartile range; RCC = renal cell carcinoma.

\*At procedure.

+Fuhrman grade 3 or 4 (G1 = well-differentiated tumour cells; G2 = moderately differentiated tumour cells; G3 = moderately to poorly differentiated tumour cells; G4 = poorly differentiated tumour cells).

‡Primary histology from pathology report.

§Patient received at least one CT of the chest or abdomen during surveillance after nephrectomy.

Intra- and postoperative medical complications¶ at their last follow-up visit for kidney cancer.

	T1	T2	Т3	Total
	(n = 1,380)	( <i>n</i> = 164)	( <i>n</i> = 438)	( <i>n</i> = 1,982)
Comparison of aggregate results				
Chest				
Observed	1,194	226	528	1,948
Recommended	1,525	418	811	2,754
Ratio of Observed vs Recommended	0.78	0.54	0.65	0.71
% of CXR	67.3	51.3	32.8	56.1
Abdomen				
Observed	2,022	294	670	2,986
Recommended	444	122	751	1,317
Ratio of Observed vs Recommended	4.55	2.41	0.89	2.27
% of US	52.5	37.4	16.6	43.0
Comparison on a per-patient basis				
Chest				
Under, %	33.2	57.3	42.7	37.3
Equal, %	46.0	31.7	37.2	42.9
Over, %	20.8	11.0	20.1	19.8
Abdomen				
Under, %	2.3	6.1	32.0	9.2
Equal, %	34.1	35.4	40.2	35.5
Over, %	63.6	58.5	27.9	55.3
Note: CXR = chest X-rays; US = ultrasound.				

#### Table 2: Compliance with the Canadian guidelines: number of tests observed versus recommended

	Chest	X-ray or	CT scan		Abdomen US or CT				
	Number of tests recommended	Under, %	Equal, %	Over, %	Number of tests recommended	Under, %	Equal, %	Over %	
T1 (n = 1,380)									
First 6	0	0	79.4	20.6	0	0	60.7	30.4	
First 12	1	33.0	51.2	15.9	0	0	40.1	59.9	
First 18	1	28.1	50.1	21.8	0	0	34.6	65.4	
First 24	2	34.5	45.6	19.9	1	4.0	37.0	59.1	
T2 ( <i>n</i> = 164)	-	51.0	10.0	17.7	1		57.0	07.1	
First 6	1	45.7	45.7	8.5	0	0	51.8	48.2	
First 12	2	52.4	34.8	12.8	1	11.6	48.8	39.6	
First 18	3	54.3	33.5	12.2	1	7.3	44.5	48.2	
First 24	4	56.1	32.3	11.6	1	4.9	39.6	59.1	
T3 ( <i>n</i> = 355)		20.1	52.5	11.0	1	1.5	59.0	07.1	
First 6	1	38.6	42.7	18.7	1	27.2	51.4	21.5	
First 12	2	40.6	38.8	20.6	2	30.8	42.7	26.5	
First 18	3	41.8	37.9	20.3	3	33.6	39.7	26.7	
First 24	4	42.9	37.2	19.9	4	34.9	38.6	26.5	

	Number of recon imaging		Number of ob- imaging		Correlation between observed and recommended chest imaging tests		
	Mean (95% CI) Median (IQ		R) Mean (95% CI) Median (IQR)		Pearson correlation	Spearman correlation	
Overall (N = 1,655)	1.34 (1.27–1.41)	1 (0–2)	1.00 (0.93-1.06)	1 (0–2)	0.55 (0.51-0.58)	0.55 (0.51-0.58)	
T1 ( <i>N</i> = 1,159)	1.05 (0.99–1.11)	1 (0–2)	0.88 (0.81-0.94)	0 (0–1)	0.52 (0.47-0.56)	0.52 (0.48-0.56)	
T2 (N = 141)	2.53 (2.17-2.87)	2(1-4)	1.32 (1.08–1.56)	1 (0–2)	0.59 (0.46-0.68)	0.60 (0.48-0.69)	
T3 (N = 355)	1.81 (1.62-2.00)	1 (0-3)	1.24 (1.09–1.39)	1 (0-2)	0.58 (0.51-0.64)	0.57 (0.48-0.62)	
	Number of recommended abdominal imaging tests		Number of obser imaging		Correlation between observed and recommended abdominal imaging tests		
	Mean (95% CI)	Median (IQR)	Mean (95% CI)	Median (IQR)	Pearson correlation	Spearman correlation	
Overall (N = 1,655)	0.65 (0.60-0.70)	0 (0–1)	1.45 (1.38–1.52)	1 (0–2)	0.47 (0.43-0.50)	0.54 (0.51-0.57)	
T1 (N = 1,159)	0.32 (0.29-0.34)	0 (0–1)	1.39 (1.31–1.47)	1 (0–2)	0.53 (0.49-0.57)	0.51 (0.47–0.56)	
T2 ( $N = 141$ )	0.78 (0.66–0.90)	1(0-1)	1.69 (1.40–1.98)	1 (0–3)	0.63 (0.52-0.72)	0.64 (0.53–0.73)	
T3 ( $N = 355$ )	1.70 (1.53–1.86)	1 (0-3)	1.56 (1.40-1.71)	1 (0-2)	0.69 (0.63-0.74)	0.71 (0.66–0.76)	

## Table 4: Level of agreement between observed versus recommended number of imaging tests in chest and abdomen

Note: CI = confidence interval; IQR = interquartile range.

	OR of the pro	bability of under-	OR of the prol	bability of over-		
	testin	g of chest	testing of abdomen			
Variable	Univariate	Multivariate OR	Univariate	Multivariate		
	OR (95% CI)	(95% CI)	OR (95% CI)	OR (95% CI)		
Men v. women	0.95 (0.76–1.17)	0.90 (0.70–1.17)	0.90 (0.74–1.11)	0.97 (0.76–1.25)		
$Age^*$ (more than 75 yr v. < 75 yr)	1.39 (1.00–1.93)	1.43 (0.96–2.12)	0.80 (0.58-1.02)	1.02 (0.68–1.51)		
High grade <sup>†</sup> (yes v. no)	0.84 (0.68–1.03)	0.67 (0.51-0.87)	0.67 (0.55-0.82)	0.97 (0.75–1.24)		
Positive surgical margin (yes	1.16 (0.78–1.75)	0.84 (0.51–1.38)	0.89 (0.60–1.32)	1.61 (0.98–2.64)		
v. no)						
Radical nephrectomy (yes v.	1.06 (0.86-1.30)	0.61 (0.45-0.82)	0.62 (0.51-0.76)	1.06 (0.80-1.39)		
no)						
Histology‡						
Other RCC	reference	reference	reference			
Low risk	1.24 (0.99–1.57)	3.14 (1.51-6.50)	0.94 (0.75–1.18)	0.69 (0.37–1.29)		
Conventional clear cell	0.89 (0.71-1.12)	2.28 (1.12-4.48)	1.08 (0.87–1.34)	0.87 (0.48–1.56)		
T1 group	reference	reference	reference	reference		
T2 group	3.00 (2.11-4.26)	5.36 (3.37-8.54)	0.90 (0.63-1.26)	0.71 (0.46–1.09)		
T3 group	1.42 (1.12–1.81)	2.64 (1.86–3.74)	0.27 (0.21-0.35)	0.23 (0.16-0.32)		
Smoking (yes v. no)	0.81 (0.60–1.09)	0.88 (0.64–1.22)	1.03 (0.78–1.36)	0.96 (0.71-1.30)		
Family history (yes v. no)	1.39 (0.90-2.07)	1.48 (0.91-2.40)	0.92 (0.61-1.39)	1.04 (0.64–1.69)		

Table 5: Factors associated with noncompliance in chest and abdominal imaging tests

Note: CI = confidence interval; OR = odds ratio; RCC = renal cell carcinoma.

\*At procedure.

+Fuhrman grade 3 or 4 (G1 = well-differentiated tumour cells; G2 = moderately differentiated tumour cells; G3 = moderately to poorly differentiated .ur ce .aomophobe RCC. tumour cells; G4 = poorly differentiated tumour cells).

Primary histology from pathology report, low-risk category includes papillary and chromophobe RCC.

Table 6:	Unit	mean/	/median	cost*	of	radiol	ogical	examinations	

	Unit mean Cost <sup>**</sup>	Unit median Cost <sup>**</sup>
Chest CT	\$613	\$400
Abdominal CT	\$627	\$428
Chest XR	\$90	\$91
<b>Abdominal US</b>	\$303	\$275

Note: BC = British Columbia; CT = computed tomography; QC = Quebec; ON = Ontario, US = ultrasound; XR = X-rays.

\*Cost is in Canadian dollars;

\*\* mean/median of the unit costs in NS, QC, ON, BC and Alberta (24-30);

Table 7: Expected and observed costs\* of surveillance over an 18-month and a 72-month period in our cohort and extrapolation for the Canadian level

	Observed	cost	Expected	cost <sup>**</sup>	Difference observed vs. expected costs						
ohort of 1,9	ohort of 1,982 patients over 18 months										
	chest	abdominal	chest	abdominal	chest	abdominal					
T1	\$326,770	\$943,217	\$403,828	\$202,020	\$-77,058	\$741,197					
T2	\$80,590	\$151,433	\$146,464	\$61,378	\$-65,874	\$90,055					
Т3	\$239,750	\$386,385	\$361,408	\$425,477	\$-121,658	\$-39,092					
Total	\$647,110	\$1,481,035	\$911,699	\$688,875	\$-264,589	\$792,160					
anadian lev	el (23,250 patients	s: 16,188 pT1; 1,	924 pT2; 5,138	pT3) over 18 mor	iths						
	chest	abdominal	chest	abdominal	chest	abdominal					
T1	\$3,833,200	\$11,064,478	\$4,737,139	\$2,369,816	\$-903,939	\$8,694,662					
T2	\$945,367	\$1,776,396	\$1,718,102	\$720,001	\$-772,735	\$1,056,395					
Т3	\$2,812,405	\$4,532,518	\$4,239,518	\$4,991,087	\$-1,427,113	\$-458,569					
Total	\$7,590,973	\$17,373,392	\$10,694,759	\$8,080,904	\$-3,103,787	\$9,292,489					
hort of 1,9	82 patients over 7	2 months									
	chest	abdominal	chest	abdominal	chest	abdominal					
T1	\$1,774,200	\$5,863,241	\$2,192,590	\$1,255,803	\$-418,389	\$4,607,438					
T2	\$284,571	\$610,697	\$517,178	\$247,525	\$-232,606	\$363,172					
Т3	\$1,165,345	\$1,352,090	\$1,756,681	\$1,488,885	\$-591,337	\$-136,795					
Total	\$3,224,116	\$7,826,028	\$4,466,448	\$2,992,213	\$-1,242,332	\$4,833,815					
anadian lev	el (23,250 patients	s: 16,188 pT1; 1,	924 pT2; 5,138	pT3) over 72 mor	iths						
	chest	abdominal	chest	abdominal	chest	abdominal					
T1	\$20,812,391	\$68,779,187	\$25,720,337	\$14,731,288	\$-4,907,946	\$54,047,900					

	chest	abdominal	chest	abdominal	chest	abdominal
T1	\$20,812,391	\$68,779,187	\$25,720,337	\$14,731,288	\$-4,907,946	\$54,047,900
T2	\$3,338,186	\$7,163,827	\$6,066,790	\$2,903,611	\$-2,728,604	\$4,260,216
Т3	\$13,670,163	\$15,860,796	\$20,606,881	\$17,465,481	\$-6,936,718	\$-1,604,685
Total	\$37,820,740	\$91,803,811	\$52,394,009	\$35,100,380	\$-14,573,269	\$56,703,431

Note:

\*Cost is in Canadian dollars; Estimations based on the mean unit costs of imaging tests.;

\*\*Based on the observed ratio of CXR vs CT chest and abdominal CT vs US (Table 2); Overall, 56.1% of performed chest examinations were CXR, and 43.0% of abdominal examinations were US.

#### References

 1. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2015. Toronto, ON: Canadian Cancer Society; 2015.

2. Mejean A, Correas JM, Escudier B, de Fromont M, Lang H, Long JA, et al. [Kidney tumors]. Prog Urol. 2007;17(6):1101-44.

3. Kane CJ, Mallin K, Ritchey J, Cooperberg MR, Carroll PR. Renal cell cancer stage migration: analysis of the National Cancer Data Base. Cancer. 2008;113(1):78-83.

4. Robson CJ, Churchill BM, Anderson W. The results of radical nephrectomy for renal cell carcinoma. J Urol. 1969;101(3):297-301.

5. Ljungberg. Guidelines on renal cell carcinoma 2014 [updated 2014. Available from: http://www.uroweb.org/gls/pdf/10\_Renal\_Cell\_Carcinoma\_LRV2.pdf.

6. Huang WC, Elkin EB, Levey AS, Jang TL, Russo P. Partial nephrectomy versus radical nephrectomy in patients with small renal tumors--is there a difference in mortality and cardiovascular outcomes? J Urol. 2009;181(1):55-61; discussion -2.

7. Russo P, Huang W. The medical and oncological rationale for partial nephrectomy for the treatment of T1 renal cortical tumors. Urol Clin North Am. 2008;35(4):635-43; vii.

8. Thompson RH, Boorjian SA, Lohse CM, Leibovich BC, Kwon ED, Cheville JC, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. J Urol. 2008;179(2):468-71; discussion 72-3.

9. Zini L, Perrotte P, Capitanio U, Jeldres C, Shariat SF, Antebi E, et al. Radical versus partial nephrectomy: effect on overall and noncancer mortality. Cancer. 2009;115(7):1465-71.

10. Huang WC, Levey AS, Serio AM, Snyder M, Vickers AJ, Raj GV, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. The lancet oncology. 2006;7(9):735-40.

11. Miller DC, Schonlau M, Litwin MS, Lai J, Saigal CS. Renal and cardiovascular morbidity after partial or radical nephrectomy. Cancer. 2008;112(3):511-20.

12. Forbes CM, Rendon RA, Finelli A, Kapoor A, Moore RB, Breau RH, et al. Disease progression and kidney function after partial vs. radical nephrectomy for T1 renal cancer. Urol Oncol. 2016.

13. Antonelli A, Cozzoli A, Nicolai M, Zani D, Zanotelli T, Perucchini L, et al. Nephronsparing surgery versus radical nephrectomy in the treatment of intracapsular renal cell carcinoma up to 7cm. Eur Urol. 2008;53(4):803-9.

14. Van Poppel H. Efficacy and safety of nephron-sparing surgery. Int J Urol. 17(4):314-26.

15. Lavallee LT, Tanguay S, Jewett MA, Wood L, Kapoor A, Rendon RA, et al. Surgical management of stage T1 renal tumours at Canadian academic centres. Can Urol Assoc J. 2015;9(3-4):99-106.

16. Janzen NK, Kim HL, Figlin RA, Belldegrun AS. Surveillance after radical or partial nephrectomy for localized renal cell carcinoma and management of recurrent disease. Urol Clin North Am. 2003;30(4):843-52.

17. Donat. Follow-up for Clinically Localized Renal Neoplasms: AUA Guideline 2013 [Available from: <u>https://www.auanet.org/education/guidelines/renal-cancer-follow-up.cfm</u>.

18. Kassouf W, Siemens R, Morash C, Lacombe L, Jewett M, Goldenberg L, et al. Follow-up guidelines after radical or partial nephrectomy for localized and locally advanced renal cell carcinoma. Can Urol Assoc J. 2009;3(1):73-6.

19. Jewett M, Finelli A, Kollmannsberger C, Wood L, Legere L, Basiuk J, et al. Management of kidney cancer: canadian kidney cancer forum consensus update 2011. Can Urol Assoc J. 2012;6(1):16-22.

20. Kim EH, Vetter JM, Kuxhausen AN, Song JB, Sandhu GS, Strope SA. Limited use of surveillance imaging following nephrectomy for renal cell carcinoma. Urol Oncol. 2015.

21. Feuerstein MA, Atoria CL, Pinheiro LC, Huang WC, Russo P, Elkin EB. Patterns of surveillance imaging after nephrectomy in the Medicare population. BJU Int. 2016;117(2):280-6.

22. Stewart SB, Thompson RH, Psutka SP, Cheville JC, Lohse CM, Boorjian SA, et al. Evaluation of the National Comprehensive Cancer Network and American Urological Association renal cell carcinoma surveillance guidelines. J Clin Oncol. 2014;32(36):4059-65.

23. Edge SB BD, Compton CC, et al, editors. AJCC cancer staging manual. 7th ed New York: Springer ed2010. p. p. 479–89.

24. Southern Alberta Institute of Urology. Internal estimates. 2016.

25. Ottawa Hospital Research Institute. Internal estimates. 2016.

26. McGill University Health Center. Internal estimates. 2016.

27. Canada Diagnostic. MRI, CT Scan, ULTRASOUND Rates British Columbia, Canada, [Available from: <u>http://www.canadadiagnostic.com/info/fees/?r=sb</u>]. 2016.

28. Radiologie Dix30. Tarification. 2016.

29. Queensway Carleton Hospital in Ottawa. Hospital Fees for Patients without Canadian Provincial or Federal Health Insurance. 2016.

30. Nova Scotia Health Authority. Internal estimates. 2016.

31. Laguna MP, Algaba F, Cadeddu J, Clayman R, Gill I, Gueglio G, et al. Current patterns of presentation and treatment of renal masses: a clinical research office of the endourological society prospective study. J Endourol. 2014;28(7):861-70.

32. Danzig MR, Weinberg AC, Ghandour RA, Kotamarti S, McKiernan JM, Badani KK. The association between socioeconomic status, renal cancer presentation, and survival in the United States: a survival, epidemiology, and end results analysis. Urology. 2014;84(3):583-9.