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Low Yield of Surveillance Imaging After Surgery for T1 Kidney Cancer

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Abstract

Purpose—To examine the mode of relapse detection and subsequent treatment after partial or radical nephrectomy in patients with low-risk (pT1, N0, Nx) kidney cancer.

Methods—Retrospective study on 1404 patients treated with partial or radical nephrectomy for low-risk kidney cancer from 2000-2012. Scans for chest imaging (X-ray or CT) and abdominal imaging (CT, MRI or ultrasound) were tabulated. For those patients with relapse, the site, mode of detection, and symptoms were recorded.

Results—Twenty-one patients relapsed with a median follow-up of 4.1 years for patients who did not relapse. In 17 (81%) patients, relapse was detected by imaging alone while 4 (19%) patients presented with symptoms. Of the patients who relapsed by imaging, 13 (76%) were treated immediately while 4 (24%) continued observation. During the first 3 years of follow-up, 5762 imaging studies were performed to detect 8 relapses, with 6 patients receiving immediate treatment. The median number of imaging studies per patient per year for the first 3 years was 1.7 (interquartile range, 1.0, 2.3) including 30% CT, 3% MRI, 36% X-ray, and 31% ultrasounds.

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Author's Contribution

Feuerstein: protocol/project development, data collection, data analysis, manuscript writing/editing; Musser: protocol/project development; data collection; data analysis; manuscript writing/editing; Kent: protocol/project development; data analysis; manuscript writing/editing; Chevinsky: data collection, manuscript editing; Cha: data collection, manuscript editing; Kimm: data collection, manuscript editing; Hilton: data collection; Sjoberg: data analysis, manuscript writing/editing; Donahue: data collection, manuscript editing; Vargas: protocol/project development, manuscript editing; Coleman: protocol/project development, Russo: protocol/project development, manuscript writing/editing

Compliance with Ethical Standards

This investigation received approval from our institution's ethical review board and was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments. Informed consent was not required (waived) by our ethical review board.

Conflict of Interest

Michael Feuerstein was supported by the National Cancer Institute/National Institutes of Health under Ruth L. Kirschstein National Research Service Award Institutional Research Training Grant T32 CA082088. Matthew Kent was supported by the Cancer Center Support Grant P30 CA008748. The contents of this manuscript are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. Paul Russo was supported by the Hanson Family Renal Cancer Research Fund, the Sidney Kimmel Center for Prostate and Urologic Cancers.

Conclusion—We found a low yield of surveillance imaging in the first 3 years for pT1 kidney cancer. Nearly 1000 imaging studies were performed to detect one relapse that required treatment. Further studies are needed to evaluate the clinical impact of imaging surveillance according to recent guidelines.

Keywords

renal neoplasm; nephrectomy; follow-up studies

Introduction

Following radical or partial nephrectomy for stage I kidney cancer, local and metastatic relapse rates range from 1-2% and 1-10%, respectively.[1] Although adjuvant systemic treatments are under active investigation in both the United States and Europe, post-operative surveillance remains the standard-of-care after the complete resection of tumor.[2]

Although history taking and physical examination are critical elements of surveillance, the rationale for surveillance imaging is to detect distant metastatic disease or local tumor recurrence before the development of signs or symptoms. It is presumed that detection of recurrence at an asymptomatic stage will allow earlier treatment, resulting in improved outcomes for the patient.

The American Urological Association (AUA) and National Comprehensive Cancer Network (NCCN) each recently released guidelines to provide a framework for kidney cancer surveillance for patients being managed by active surveillance, surgical resection, and thermal ablative therapies.[2-3] Prior to these guidelines, post-operative surveillance protocols were based on recurrence patterns reported in retrospective series.[4-9] However, the detection rates of imaging and impact on clinical decision-making have not been widely studied. Our objective was to examine the mode of relapse detection and subsequent treatment in patients with low-risk (pT1, N0, Nx) disease.

Methods

Our cohort consisted of 1821 patients treated with radical or partial nephrectomy for stage pT1 kidney cancer at our center from the years 2000-2012. Patients with synchronous, bilateral disease were excluded in our initial search. After removing patients with another cancer diagnosis (n=417) who might undergo surveillance testing for reasons other than kidney cancer, our final cohort included 1404 patients. Scans for chest imaging (X-ray or CT) and abdominal imaging (CT, MRI or ultrasound) were documented from our internal records as well as all available outside records. Scans performed after relapses were not included in our analysis.

For those patients documented as having a local or distant relapse, the site, mode of detection, and symptoms at relapse were recorded. When pathological confirmation of a relapse was not available, we relied on imaging and chart review. When relapse was detected, we determined the date of relapse and what additional treatment was received.

The minimum time period of surveillance recommended by the AUA and NCCN guidelines is 3 years.[2, 3] Hence, we conducted an analysis in which we calculated the rate of chest and abdominal imaging studies per year received by each patient for the first 3 years. The average number of imaging studies for patients with less than 3 years of follow-up and patients relapsing within 3 years were calculated until the last follow-up date or date of relapse. We hypothesized that patients would receive imaging studies more frequently based on procedure type or more aggressive disease. To test this hypothesis, we created a multivariable linear regression model for the rate of studies a patient received for the first 3 years adjusted for procedure type (partial vs. radical nephrectomy), pathological grade (1/2 vs. 3/4), stage (pT1A vs. pT1B), and tumor size (largest dimension). All statistical analyses were performed using Stata 12.0 (StataCorp, College Station, TX).

Results

Table 1 presents the cohort characteristics. In total, 21 patients had a relapse with a median follow-up of 4.1 years for patients who did not relapse (Supplemental table).

Seventeen (81%) of the relapses were found by imaging alone while 4 (19%) patients presented with symptoms (Table 2). Of the 17 patients with relapse detected by imaging, 13 (76%) underwent immediate treatment while 4 (24%) were managed with observation. Figure 1 is a visual representation of when patients relapsed and how relapse was detected.

When we examined only the first 3 years of follow-up, 5762 imaging studies were performed on 1404 patients. The median number of studies per year per patient was 1.7 (interquartile range, IQR, 1.0, 2.3). The breakdown of types of studies was 30% CT scans, 3% MRIs, 36% X-rays, and 31% ultrasounds. A total of 10 relapses were detected, including 8 by imaging alone and 2 by symptoms. Six of 8 patients with a relapse detected by imaging received immediate treatment.

Additionally, we repeated our analyses looking at the rates of imaging for partial and radical nephrectomy patients separately. We found that for partial nephrectomy patients, 4936 imaging studies were performed on 1181 patients. The median number of studies per year per patient was 1.7 (IQR 1.0, 2.3). The breakdown of studies was 30% CT, 3% MRI, 35% X-rays, and 32% ultrasounds. A total of five relapses were detected by imaging with four of those patients receiving treatment. For radical nephrectomy patients, 826 imaging studies were performed on 223 patients. The median number of studies per year per patient was 1.3 (IQR 0.66, 1.9). The breakdown of studies was 37% CT, 4% MRI, 40% X-rays, and 20% ultrasounds. A total of three relapses were detected by imaging with two of those patients receiving treatment.

We found that baseline risk and procedure type were associated with the rate of imaging studies received in the first 3 years. There was a statistically significant association between rate of studies and higher pathological grade (Beta = 0.29 [95% CI 0.10, 0.48]; $p = 0.003$), higher pathological stage (Beta = 0.40 [95% CI 0.05, 0.75]; $p = 0.027$), and receiving a radical nephrectomy (Beta = -0.28 [95% CI -0.54, -0.03]; $p = 0.030$). However, when tumor size was examined as a continuous variable, patients with smaller tumors received

more surveillance imaging (Beta = -0.11 [95% CI -0.22, -0.004]; p = 0.059) but this did not reach conventional levels of statistical significance.

Discussion

There is good evidence from retrospective studies that relapse after nephrectomy is closely associated with pathological stage and that the chest is the most common site of relapse.[4-9] These studies each developed specific follow-up protocols for surveillance based on patterns of relapse, and only 1 recommended abdominal imaging for surveillance after nephrectomy for low-stage disease.[9] These studies did not distinguish different protocols based on type of nephrectomy, radical or partial, performed. However, recent population-based studies have demonstrated tremendous variability in the use of surveillance imaging, suggesting that physicians did not widely accept these protocols.[10, 11]

Recent AUA and NCCN guidelines recommend no more than annual chest imaging in the first 3 years and abdominal imaging in the first year followed by annually only at the discretion of the physician based on individual patient risk factors.[2, 3] While the NCCN guidelines recommend similar protocols for radical and partial nephrectomy, the AUA guidelines recommend cross-sectional imaging in the first year after partial nephrectomy and ultrasound, CT or MRI in the first year after radical nephrectomy. It should be noted that this is based on expert opinion with no available supportive evidence.

In the current study, we found a very low yield of surveillance imaging, particularly in the first 3 years after surgery. More than 5,500 imaging studies were performed on 1,404 patients to detect 8 asymptomatic relapses, only 6 of which were treated. In other words, only 1 in 1000 studies led to a clinical action. Interestingly, 11 of 21 relapses occurred after the 3-year cut-off recommended by the NCCN and AUA. This would argue for a longer duration of surveillance than is recommended by current guidelines.

To our knowledge, only one other study has examined the detection rate of relapse by imaging after nephrectomy.[12] Similar to our study, the authors found a high rate of relapses beyond 3 years. In contrast to our findings, these authors found that current guidelines will miss a large number of relapses, particularly for low-risk patients and patients with abdominal relapses. Unfortunately, this study did not examine whether relapses could have been detected by symptoms or whether relapse detection would have affected clinical decision-making. This study is also notable for a higher rate of relapse than would be expected for low-risk disease, perhaps due to inclusion of patients dating back to 1970.[1]

We cannot necessarily assume that earlier detection of asymptomatic relapse portends a better outcome.[13] In fact, a substantial proportion of patients with relapse will have an indolent clinical course, although a relapse detected within the first year after surgery is a poor prognostic variable.[14] Distinguishing patients at risk for early relapse following surgery could further direct the use of imaging, as well as adjuvant and salvage therapies.

We believe that our findings support more judicious use of imaging surveillance. Intensive imaging for low-risk patients may be a source of unnecessary radiation and healthcare expenditures. Considering the use of abdominal CT, there is a linear dose-response

relationship between ionizing radiation exposure and risk of solid cancers or leukemia.[15] A recent review estimated 10-year cumulative radiation exposure of different kidney cancer surveillance protocols.[16] This study found significant variability in cumulative exposure, with some protocols exposing patients to well over 100 mSv, a level that has been associated with a 7.6% attributable risk of carcinogenesis. Although a wide variability of radiation doses from CT examinations and the decreased risk of carcinogenesis with increasing age of exposure have been reported, our findings support decreased use of radiation.[17] We did not examine the development of secondary cancers in the current study. Patients with another cancer diagnosis were excluded to avoid counting diagnostic or surveillance imaging performed for another cancer.

Unnecessary tests also have important cost implications. From the mid-1990s through the mid-2000s, use of advanced imaging among Medicare beneficiaries grew by more than 6 percent per year[18], and increases in imaging costs outpaced the rate of increase of all other costs in cancer care[19]. This was in part due to self-referrals among physicians who part owned advanced imaging facilities such as CT or MRI.[20] During the time period of this study, only one single-center experience recommended cross-sectional chest imaging over chest X-ray in surveillance.[9] Fortunately, there are some signs that this growth in imaging costs is slowing, possibly due to efforts to reduce the use of tests with unproven medical value.[18]

Some providers may order imaging studies to put patients more at ease. In fact in breast cancer, more frequent surveillance imaging is associated with worse patient-reported quality-of-life, increased costs and no benefit in overall survival.[21]

We acknowledge that there are limitations to our analysis. The retrospective nature of the study likely underestimates the true number of imaging studies. The number and type of studies used were at the discretion of the treating physician prior to any published surveillance guidelines. While we excluded patients with another known cancer or bilateral, synchronous disease, we did not control for other benign conditions associated with imaging during the surveillance period.

In the absence of any prospective data, this is one of the first studies to evaluate the yield of surveillance imaging for detecting asymptomatic relapses and the subsequent affect on clinical decision-making. In this large cohort, we found that imaging alone detected few relapses that necessitated immediate treatment. We hope that the dissemination of AUA and NCCN surveillance guidelines will lead to a reduction in the number of unnecessary imaging studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Number at risk

1404 1264 1060 885 721 562 452 347 252 185 117

Figure 1.
Risk of relapse by mode of detection. 3-year line provided as cutoff of imaging guidelines.
(Gray = Radiology, Black = Symptomatic)

Table 1

Patient characteristics.

	N=1404
Patient Age	58.3 (49.4, 67.3)
Patient Race (N=1804)	
White	1266 (91%)
African-American	60 (4.3%)
Asian	45 (3.2%)
Other	18 (1.3%)
ASA Score	
I/II	835 (59%)
III/IV	569 (41%)
Pathological Grade (N=1045)	

All values are median (IQR) or frequency (%)

Table 2

Anatomic location and mode of detection of relapses.

G1	84 (8.0%)
G2	614 (59%)
G3	336 (32%)
G4	10 (1.0%)
Pathological Stage	
T1A	1019 (73%)
T1B	385 (27%)
Pathological Tumor Size	3.0 (2.1, 4.3)
Tumor Presentation (N=1398)	
Incidental	1171 (84%)
Local	215 (15%)
Systemic	11 (0.8%)
Year of Surgery	
2000 - 2003	276 (20%)
2004 - 2007	405 (29%)
2008 - 2012	723 (51%)
Type of Surgery	
Radical Nephrectomy	1181 (84%)
Partial Nephrectomy	223 (16%)

	Mode of Detection				
Location	Symptoms	Ultrasound	Chest X-ray	CT scan	MRI
Abdominal/Retroperitoneal	0 (0%)	1 (20%)	0 (0%)	4 (80%)	0 (0%)
Chest	1 (9%)	0 (0%)	3 (27%)	7 (64%)	0 (0%)
Other	3 (60%)	1 (20%)	0 (0%)	0 (0%)	1 (20%)