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Long-term risk of recurrence in surgically treated intermediate-high risk renal cell carcinoma: a post-hoc analysis of the Eastern Cooperative Oncology Group - American College of Radiology Imaging Network E2805 Trial cohort

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Long-term risk of recurrence in surgically treated intermediate-high risk renal cell carcinoma: a post-hoc analysis of the Eastern Cooperative Oncology Group - American College of Radiology Imaging Network E2805 Trial cohort

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Introduction

- **Surgical resection remains the gold standard treatment for clinically localized renal cell carcinoma (RCC)**
- **Rates of recurrence continue to remain significant – estimations noted to range from 20 – 30 %**
- **Most contemporary guidelines use risk-stratified models as a foundation for post-operative surveillance recommendations**
- **The guidelines for post-operative surveillance are clear and structured for patients within the first 5 years following surgery**
- **There are no clear indications nor instruction for the follow-up protocols following 5 years after surgery**



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 preferred) 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
- Bone scan, as clinically indicated

^aDonat SM, Diaz M, Bishoff JT, et al. Follow-up for clinically localized renal neoplasms: AUA Guideline. J Urol 2013;190:407-416

^bNo single follow-up plan is appropriate for all patients. Follow-up frequency and duration should be individualized based on patient characteristics and clinical judgment. Further study is required to define optimal follow-up duration.



Risk profile	Surveillance				
	6 mo	1 y	2 y	3 y	> 3 y
Low	US	CT	US	CT	CT once every 2 years; Counsel about recurrence risk of ~10%
Intermediate / High	CT	CT	CT	CT	CT once every 2 years



Surgery. Moderate to High Risk Patients (pT2-4N0 Nx or any stage N+):

12. The Panel recommends that moderate to high risk patients undergo baseline chest and abdominal scan (CT or MRI) within three to six months following surgery with continued imaging (US, CXR, CT or MRI) every six months for at least three years and annually thereafter to year five. (*Recommendation*; Evidence Strength. Grade C)

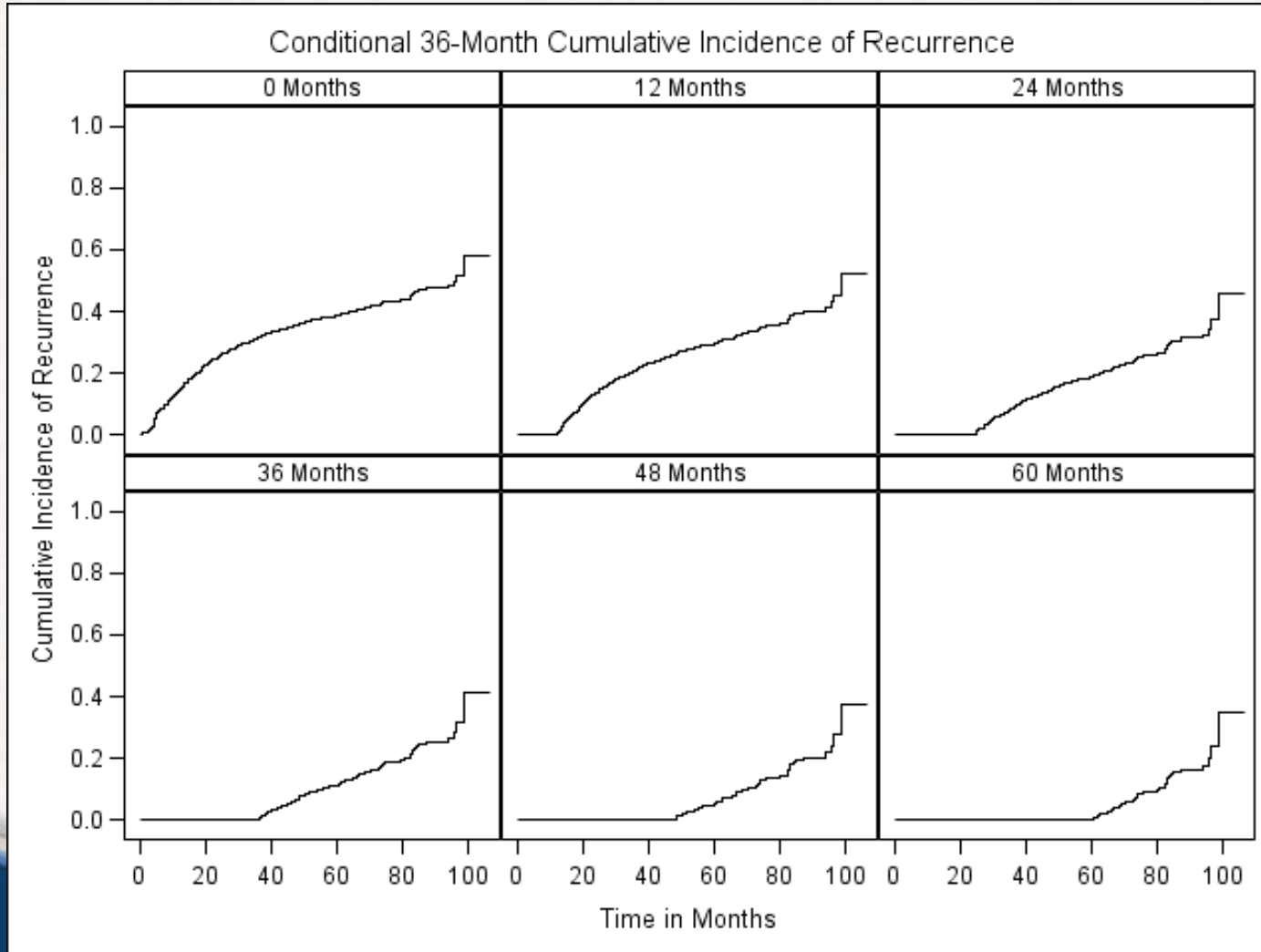
13. The Panel recommends site-specific imaging as warranted by clinical symptoms suggestive of recurrence or metastatic spread. (*Recommendation*; Evidence Strength. Grade C)

14. Imaging (US, CXR, CT or MRI) beyond five years may be performed at the discretion of the clinician for moderate to high risk patients. (*Option*; Evidence Strength. Grade C)

Methods

- **Patient Cohort:** Post-hoc analysis of 1,943 total patients within Eastern Cooperative Oncology Group - American College of Radiology Imaging Network (ECOG-ACRIN) E2805 Trial cohort
- **Primary Outcome:** Rates of recurrence following surgical resection
 - Post-operative recurrence rates determined using cumulative incidence
 - 36-month rates of recurrence assessed for patients whom did not have recurrence at sequential intervals following surgery
- **Secondary Outcome:** Clinical and pathological features predictive of recurrence at 0-months and 60-months
 - Covariates: age, sex, race, T stage, N stage, M stage, Fuhrman grade, histology, surgical approach (open vs. laparoscopic), type of nephrectomy (nephron-sparing vs. radical), ECOG performance status

Results



- Median (IQR) age was 56 (49 - 64)
- 730 patients developed recurrence
- T3/T4 (58.8%) most common
- Most underwent radical nephrectomy (95.0%)
- Majority underwent open approach (57.1%)
- 36-month cumulative incidence of recurrence
 - 0 months - 31.1%
 - 12 months - 26.0%
 - 24 months - 18.8%
 - 36 months - 16.1%
 - 48 months - 18.9%
 - 60 months - 20.3%

Results

Multivariate Competing Risks at 0 - months

Variable	HR (CI)	P-Value
Sex		
Male	1.23 (1.04 - 1.45)	0.0169
Female		
Age	1.01 (1 - 1.01)	0.1207
ECOG Performance Score		
1	1.17 (0.98 - 1.4)	0.0785
0		
Surgical Approach		
Laparoscopic	0.81 (0.69 - 0.95)	0.0114
Open		
Histology		
Clear Cell	1.2 (0.96 - 1.5)	0.1009
Non-clear cell		
Pathologic T Stage		
T1		
T2	1.48 (1.09 - 2.03)	0.0134
T3 & 4	1.74 (1.3 - 2.31)	0.0002
Pathologic N Stage		
N0	1.1 (0.92 - 1.31)	0.2817
N1 & 2	2.38 (1.85 - 3.07)	<0.0001
Nx		
Pathologic M Stage		
M0	0.76 (0.63 - 0.92)	0.0054
Mx		
Fuhrman Grade		
4	2.36 (1.92 - 2.9)	<0.0001
3	1.36 (1.14 - 1.62)	0.0007
1 & 2		

ECOG: Eastern Cooperative Oncology Group; CI: Confidence Interval

Multivariate Competing Risks at 60 - months

Variable	HR (CI)	P-Value
Sex		
Male	1.63 (0.89 - 2.96)	0.1107
Female		
Age	1.01 (0.99 - 1.03)	0.4310
Pathologic T Stage		
T1		
T2	0.76 (0.3 - 1.88)	0.5500
T3 & 4	1.04 (0.48 - 2.28)	0.9161
Pathologic N Stage		
N0	0.66 (0.37 - 1.18)	0.1594
N1 & 2	2.36 (0.88 - 6.33)	0.0870
Nx		
Pathologic M Stage		
M0	0.76 (0.63 - 0.92)	0.0054
Mx		
Fuhrman Grade		
4	1.23 (0.53 - 2.86)	0.6304
3	1.42 (0.77 - 2.6)	0.2628
1 & 2		

CI: Confidence Interval

Conclusions

Our results support the necessity of long-term follow-up in all intermediate- to high-risk RCC patient whom were treated surgically. Although the exact duration and stop date of follow-up remains to be established, the data supports follow-up beyond 5-years and likely up to 8 years following surgery. Larger prospective studies are still required to identify the optimal surveillance protocol and duration of follow-up