Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin.* 2015;65(1):5-29.	Review/Other-Tx	N/A	To provide the expected numbers of new cancer cases and deaths in 2015 nationally and for each state, as well as a comprehensive overview of cancer incidence, mortality, and survival rates and trends using the most current population-based data. The article also estimates the total number of deaths averted nationally during the past 2 decades and by state in 2011 as a result of the continual decline in cancer death rates and present actual number of deaths reported in 2011 by age for the 10 leading causes of death and for the 5 leading causes of cancer death.	Cancer death rates have been continuously declining for the past 2 decades. Overall, the risk of dying from cancer decreased by 22% between 1991 and 2011. Regionally, progress has been most rapid for residents of the Northeast, among whom death rates have declined by 25% to 30%, and slowest in the South, where rates declined by about 15%. Further reductions in cancer death rates can be accelerated by applying existing cancer control knowledge across all segments of the population, with an emphasis on those in the lowest socioeconomic bracket and other disadvantaged populations.	4
2. King SC, Pollack LA, Li J, King JB, Master VA. Continued Increase in Incidence of Renal Cell Carcinoma, Especially in Young Patients and High Grade Disease: United States 2001 to 2010. *J Urol.* 2014;191(6):1665-1670.	Review/Other-Dx	342,501 RCC cases diagnosed	To examine invasive, microscopically confirmed kidney and renal pelvis cancers diagnosed from 2001 to 2010 that met United States Cancer Statistics reporting criteria for each year, excluding cases diagnosed by autopsy or death certificate.	A total of 342,501 RCC cases were diagnosed. The RCC incidence rate increased from 10.6/100,000 individuals in 2001 to 12.4/100,000 in 2010 and increased with age until ages 70 to 74 years. The incidence rate in men was almost double that in women. The annual percent change was higher in women than in men, in those 20 to 24 years old and in grade III tumors.	4
3. National Cancer Data Base (NCDB). http://www.facs.org/cancer/ncdb/index.html. Accessed September 30, 2015.	Review/Other-Dx	N/A	An article about the National Cancer Data Base.	No results stated.	4
4. Leslie JA, Prihoda T, Thompson IM. Serendipitous renal cell carcinoma in the post-CT era: continued evidence in improved outcomes. *Urol Oncol.* 2003;21(1):39-44.	Observational-Dx	257 patients	To compare patient and tumor characteristics between serendipitous and nonserendipitously discovered RCC in the recent widespread use of CT and US. Tumor registry was reviewed for diagnosis and treatment of RCC.	Use of CT and US has led to the discovery of many asymptomatic lesions, including renal tumors.	2
5. Flanigan RC, Campbell SC, Clark JI, Picken MM. Metastatic renal cell carcinoma. *Curr Treat Options Oncol.* 2003;4(5):385-390.	Review/Other-Dx	N/A	To review management of patients with metastatic RCC.	Metastases may be found at diagnosis or at some interval after nephrectomy. A shorter interval between nephrectomy and the development of metastases is linked with poorer prognosis. Patients with metastatic RCC face a dismal prognosis, with a median survival time of only 6 to 12 months and a 2-year survival rate of 10% to 20%.	4
6. Griffin N, Gore ME, Sohaib SA. Imaging in metastatic renal cell carcinoma. *AJR Am J Roentgenol.* 2007;189(2):360-370.	Review/Other-Dx	N/A	To review the role of imaging in metastatic RCC.	Imaging is likely to play an increasing role in the management, diagnosis, and monitoring of response to treatment of metastatic RCC.	4

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7. Scoll BJ, Wong YN, Egleston BL, Kunkle DA, Saad IR, Uzzo RG. Age, tumor size and relative survival of patients with localized renal cell carcinoma: a surveillance, epidemiology and end results analysis. *J Urol.* 2009;181(2):506-511.	Observational-Tx	8,578 patients	To analyze data from the SEER (Surveillance, Epidemiology and End Results) database to evaluate the relative survival of patients treated surgically for localized RCC as related to tumor size and patient age.	A total of 8,578 patients with surgically treated, localized RCC were identified. While 3 and 5-year survival for patients with small (<4 cm) RCC was no different from that of matched cancer-free controls, patients treated for large (>7 cm) localized RCC experienced decreased 5-year relative survival across all age groups. Therefore, age was not a significant predictor of relative survival for patients with small (<4 cm) or large (>7 cm) tumors. However, a statistically significant trend toward lower relative survival with increasing age was demonstrated in patients with medium size tumors (4 to 7 cm). Hypothesis testing confirmed these findings.	2
8. Edge SB, Byrd DR, Compton CC, et al. *AJCC Cancer Staging Manual (7th Edition)*. New York, NY: Springer; 2010.	Review/Other-Tx	N/A	AJCC Cancer Staging Manual.	N/A	4
9. Frank I, Blute ML, Leibovich BC, Cheville JC, Lohse CM, Zincke H. Independent validation of the 2002 American Joint Committee on cancer primary tumor classification for renal cell carcinoma using a large, single institution cohort. *J Urol.* 2005;173(6):1889-1892.	Review/Other-Dx	2,746 patients	To evaluate the 2002 primary tumor classification and compare its predictive ability with that of the 1997 classification.	2002 primary tumor classification with pT1 cancers sub-classified into pT1a and pT1b provides excellent stratification of patients according to cancer specific survival and it has a predictive ability that is superior to that of the 1997 classification.	4
10. Nese N, Paner GP, Mallin K, Ritchey J, Stewart A, Amin MB. Renal cell carcinoma: assessment of key pathologic prognostic parameters and patient characteristics in 47,909 cases using the National Cancer Data Base. *Ann Diagn Pathol.* 2009;13(1):1-8.	Review/Other-Dx	47,909 RCCs	To describe the disease characteristics and use of conventional prognostic parameters in a hospital-based cohort of pathologically confirmed RCCs.	The 5-year observed survival of RCC was 62.9% for male and 68.1% for female and was 81.0% for <40 years old and 64.2% for >40 years old. The 5-year observed survival of RCC patients by the fifth edition 1997 AJCC TNM staging were stages I, 77.8%; II, 72.8%; III, 55.0%; and IV, 16.9%, demonstrating a dramatic decline in patient survival at stage IV. By reported pathologic grade, significant stratification was achieved in the observed survival for RCC overall irrespective of histologic subtypes (grade 1, 77.8%; 2, 69.6%; 3, 48.8%; and 4, 35.3% 5-year observed survival).	4

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11. Yoo C, Song C, Hong JH, Kim CS, Ahn H. Prognostic significance of perinephric fat infiltration and tumor size in renal cell carcinoma. *J Urol.* 2008;180(2):486-491; discussion 491.	Observational-Tx	783 patients with pT1-2 (cN0M0) and 77 patients with pT3a (cN0M0) RCC	To evaluate the influence of perinephric fat infiltration and tumor size on patient survival.	Patients with pT1-2 and pT3a tumors had a 5-year cancer specific survival rate of 96.1% and 84.9%, and a 5-year disease-free survival rate of 93.4% and 74.7%, respectively (each $P<0.01$). Age, tumor size and Fuhrman nuclear grade were independent prognostic factors for cancer specific and disease-free survival, whereas perinephric fat infiltration was significant only for disease-free survival. However, perinephric fat infiltration had a significant effect on cancer specific survival in patients with pT3a tumors >7 cm ($P=0.001$). In contrast, patients with pT3a tumors ≤7 cm had cancer specific and disease-free survival similar to that of patients with pT2 tumors. Recurrence of pT3a tumors >7 cm was observed in 44% of patients but in only 14.6% of those with pT3a tumors ≤7 cm ($P=0.029$). In contrast to the recurrence of tumors ≤7 cm, recurrence of pT3a tumors >7 cm usually developed at multiple sites with a large tumor burden and it progressed rapidly. Consequently 85% of patients with recurrence of pT3a tumors >7 cm died of RCC compared with 33% of those with recurrence of pT3a tumors ≤7 cm ($P=0.001$).	2
12. Park WH, Eisen T. Prognostic factors in renal cell cancer. *BJU Int.* 2007;99(5 Pt B):1277-1281.	Review/Other-Dx	N/A	Review prognostic factors in RCC.	No results stated in abstract.	4
13. Raj GV, Thompson RH, Leibovich BC, Blute ML, Russo P, Kattan MW. Preoperative nomogram predicting 12-year probability of metastatic renal cancer. *J Urol.* 2008;179(6):2146-2151; discussion 2151.	Review/Other-Dx	2,517 patients	To develop a nomogram that predicts the likelihood of metastatic recurrence following partial or radical nephrectomy.	Metastatic recurrence developed in 340/2,517 patients. Median follow up for patients without metastatic recurrence was 4.7 years. A nomogram was developed using preoperative characteristics to predict the 12-year likelihood of postoperative metastatic recurrence with a concordance index of 0.80. In contrast, the concordance index of preoperative TNM staging was 0.71. Size of the primary renal mass, evidence of lymphadenopathy or necrosis on preoperative imaging and the mode of presentation were important predictors for the subsequent development of metastases.	4

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14. Sorbellini M, Kattan MW, Snyder ME, et al. A postoperative prognostic nomogram predicting recurrence for patients with conventional clear cell renal cell carcinoma. *J Urol.* 2005;173(1):48-51.	Observational-Dx	701 patients	To develop and perform external validation of a postoperative nomogram to predict recurrence after surgery for conventional clear cell renal cortical carcinomas.	Disease recurrence was noted in 72/701 patients. Those patients without evidence of disease had a median and maximum follow-up of 32 and 120 months, respectively. The 5-year probability of freedom from recurrence for the patient cohort was 80.9% (95% CI, 75.7% to 85.1%). A nomogram was designed based on a Cox proportional hazards regression model. Following external validation predictions by the nomogram appeared accurate and discriminating, and the concordance index was 0.82.	3
15. Suzuki K, Nishiyama T, Hara N, Akazawa K, Takahashi K. Kattan postoperative nomogram for renal cell carcinoma: predictive accuracy in a Japanese population. *Int J Urol.* 2011;18(3):194-199.	Observational-Dx	211 patients	To establish the predictive accuracy of the Kattan postoperative nomogram for nonmetastatic RCC in a Japanese population.	The 5-year RFS rate for all patients calculated using the Kaplan-Meier method was 80.6%. In multivariate analysis, the statistically significant prognostic factors for 5-year RFS were high-grade tumors (P=0.019) and symptomatic disease (P=0.017). The concordance index for RFS predicted by the Kattan nomogram was 0.735 (95% CI: 0.734–0.736). There was a slight discrepancy between the RFS predicted by the Kattan nomogram and the likelihood of being recurrence-free at 5 years according to the Cox analysis in the current patient population.	2
16. Comprehensive molecular characterization of clear cell renal cell carcinoma. *Nature.* 2013;499(7456):43-49.	Review/Other-Dx	N/A	To evaluate clinical and pathological features, genomic alterations, DNA methylation profiles, and RNA and proteomic signatures in clear cell RCC.	No results stated in abstract.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
17. Joseph RW, Kapur P, Serie DJ, et al. Loss of BAP1 protein expression is an independent marker of poor prognosis in patients with low-risk clear cell renal cell carcinoma. *Cancer*. 2014;120(7):1059-1067.	Observational-Dx	1,479 patients	A highly sensitive and specific immunohistochemistry assay was used to test whether BAP1 expression is an independent marker of clear cell RCC-specific survival, particularly in patients with low-risk disease.	A total of 10.5% of tumors were BAP1-negative, 84.8% of tumors were BAP1-positive, and 4.6% of tumors had ambiguous staining for BAP1. Patients with BAP1-negative tumors have an increased risk of clear cell RCC-related death (HR = 3.06; 95% CI, 2.28–4.10; *P*=6.77 x 10(-14)). BAP1 expression remained an independent marker of prognosis after adjusting for the UCLA integrated staging system (HR = 1.67; 95% CI, 1.24–2.25; *P*<.001). Finally, BAP1 was an independent prognostic marker in low-risk patients with a Mayo Clinic stage, size, grade, and necrosis score of ≤3 (HR = 3.24; 95% CI, 1.26-8.33; *P*=.015).	3
18. Kapur P, Pena-Llopis S, Christie A, et al. Effects on survival of BAP1 and PBRM1 mutations in sporadic clear-cell renal-cell carcinoma: a retrospective analysis with independent validation. *Lancet Oncol*. 2013;14(2):159-167.	Observational-Tx	145 patients	To investigate the clinicopathological significance of BAP1 and PBRM1 mutations and to determine whether patients with BAP1-mutant and PBRM1-mutant tumors had different overall survival.	The median overall survival in the UTSW cohort was significantly shorter for patients with BAP1-mutant tumors (4.6 years; 95% CI, 2.1–7.2), than for patients with PBRM1-mutant tumors (10.6 years; 9.8–11.5), corresponding to a HR of 2.7 (95% CI, 0.99–7.6, *P*=0.044). Median overall survival in the TCGA cohort was 1.9 years (95% CI, 0.6–3.3) for patients with BAP1-mutant tumors and 5.4 years (4.0–6.8) for those with PBRM1-mutant tumors. A HR similar to the UTSW cohort was noted in the TCGA cohort (2.8; 95% CI, 1.4–5.9; *P*=0.004). Patients with mutations in both BAP1 and PBRM1, although a minority (3 in UTSW cohort and 4 in TCGA cohort), had the worst overall survival (median 2.1 years, 95% CI, 0.3–3.8, for the UTSW cohort, and 0.2 years, 0.0–1.2, for the TCGA cohort).	2

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19. Klatte T, Patard JJ, de Martino M, et al. Tumor size does not predict risk of metastatic disease or prognosis of small renal cell carcinomas. *J Urol.* 2008;179(5):1719-1726.	Observational-Tx	1,208 patients	To characterize the clinicopathological features and the prognosis of small solid renal tumors defined as tumors ≤4 cm.	Of the tumors 88% were RCC and 12% were benign. Of those with RCC, 995 (93%) were localized (N0M0) and 72 (7%) presented with metastatic disease. Tumor size did not predict synchronous metastatic disease. The incidence of metastatic disease in the tumor size ranges 0.1 to 1.0, 1.1 to 2.0, 2.1 to 3.0 and 3.1 to 4.0 cm was 7%, 6%, 5% and 8%, respectively (*P*=0.322). Survival rates were excellent. The majority of patients who died of RCC (54%) presented with synchronous metastatic disease, but 3% of patients with localized disease also died of RCC. In patients with localized disease there was a 7% chance of recurrence post nephrectomy at 5 years. Progression-free survival (28 months) was better than for patients with metastatic disease having a primary tumor >4 cm (8 months). Tumor size was not retained as an independent prognostic factor of survival in multivariate analyses. The University of California Integrated Staging System and the Karakiewicz nomogram were the best predictors of cancer specific survival for all RCC stages (c-index 0.87).	2
20. Guethmundsson E, Hellborg H, Lundstam S, Erikson S, Ljungberg B. Metastatic potential in renal cell carcinomas </=7 cm: Swedish Kidney Cancer Quality Register data. *Eur Urol.* 2011;60(5):975-982.	Review/Other-Dx	2,033 patients	To evaluate the incidence of local T-category distribution and lymph node and distant metastases in relation to tumor size in RCCs ≤7 cm in a nationally based patient population.	Most RCCs were discovered incidentally and incidence correlated inversely to tumor size. There were 887 (43%) patients with category T1a tumors, 836 (40%) with category T1b, 174 (8%) with T3a, 131 (6%) with T3b/c, and 12 (1%) patients had invasion of adjacent organs (T4). A total of 309 (15%) patients had lymph node and/or distant metastases. Of the 177 1- to 2-cm RCCs, category T3 tumors were identified in 3 patients and lymph node and/or distant metastases were identified in 8 (5%). Only for tumors ≤1 cm was there neither advanced stage nor metastasis. The occurrence of locally advanced growth, lymph node and distant metastases, and high tumor grade correlated to tumor size. Patients with Fuhrman grade III or IV had a four-fold greater risk of metastases than grades I or II.	4

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21. Steffens S, Junker K, Roos FC, et al. Small renal cell carcinomas--how dangerous are they really? Results of a large multicenter study. *Eur J Cancer.* 2014;50(4):739-745.	Review/Other-Dx	2,197 patients	To evaluate the prevalence of risk factors such poor tumor differentiation and synchronous metastases in patients with small RCC (64 cm).	At the time of surgery, tumors were staged as pT3a in 175 (8.0%) cases, 134 (6.2%) were poorly differentiated and 75 (3.5%) were metastasized. The larger the tumor size, the higher was the risk of presenting with stage pT3a (P<0.001), poor tumor differentiation (P=0.004), microscopic vascular involvement (P=0.001) and collecting system invasion (P=0.03). The 5-year cancer-specific survival rate was 93.8% for stage pT1a vs 79.4% for stage pT3a (P<0.001), and it was 93.7% for Grade 1-2 vs 76.8% for Grade 3-4 differentiation (P<0.001). Multivariate analysis identified age in years (HR 1.04, P<0.001), metastatic disease (HR 12.5, P<0.001), tumor differentiation (HR 2.8, P<0.001) and nonclear cell histology (HR 0.51, P=0.02) as independent prognosticators for cancer-specific survival rate in patients with small RCC. Interestingly, the 5-year cancer-specific mortality rate for pT1a N/M0 patients was 5.8%.	4
22. Tsui KH, Shvarts O, Smith RB, Figlin RA, deKernion JB, Belldegrun A. Prognostic indicators for renal cell carcinoma: a multivariate analysis of 643 patients using the revised 1997 TNM staging criteria. *J Urol.* 2000;163(4):1090-1095; quiz 1295.	Observational-Dx	643 consecutive patients	Retrospective review to determine independent prognostic indicators for RCC using the revised 1997 TNM staging criteria.	The 5-year cancer specific survival rate was 91%, 74%, 67% and 32% for TNM stages I, II, III and IV lesions, respectively (p<0.001). Analysis demonstrated a survival rate of 83% for stage T1, 57% for stage T2, 42% for stage T3 and 28% for stage T4 disease (p<0.001), and 89% for grade 1, 65% for grade 2, and 46% for grades 3 and 4 (p<0.001). Multivariate analysis revealed that overall TNM stage and grade of disease were the most important prognostic indicators for renal cell carcinoma (p<0.001). ECOG classification was a less significant predictor (p = 0.031) and tumor stage was not shown to have any independent impact on patient survival (p = 0.138).	2

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23. Seute T, Leffers P, ten Velde GP, Twijnstra A. Detection of brain metastases from small cell lung cancer: consequences of changing imaging techniques (CT versus MRI). *Cancer.* 2008;112(8):1827-1834.	Observational-Dx	481 consecutive patients	To show 1) the effect of changing from CT to MRI on the prevalence of detected brain metastases in patients with newly diagnosed small cell lung cancer; 2) the difference in survival between patients with single and multiple brain metastases; and 3) the effect of the change in patient labeling on eligibility for prophylactic brain irradiation.	The prevalence of detected brain metastases was 10% in the CT era and 24% in the MRI era. In the CT era, all detected brain metastases were symptomatic, whereas in the MRI era, 11% were asymptomatic. In both periods, patients labeled as single brain metastases survived longer than those labeled as multiple brain metastases. For patients labeled as single brain metastases or multiple brain metastases, survival was longer in the MRI era than in the CT era. The proportion of patients who were eligible for prophylactic cranial irradiation was lower in the MRI era.	3
24. Kuhn MJ, Hammer GM, Swenson LC, Youssef HT, Gleason TJ. MRI evaluation of "solitary" brain metastases with triple-dose gadoteridol: comparison with contrast-enhanced CT and conventional-dose gadopentetate dimeglumine MRI studies in the same patients. *Comput Med Imaging Graph.* 1994;18(5):391-399.	Review/Other-Dx	4 patients	To compare the sensitivity and safety of high dose gadoteridol (Pro Hance) with routine dose gadopentetate dimeglumine (Magnevist) in the detection of intracranial metastases on MRI when a solitary intracranial lesion was detected on contrast-enhanced cranial CT.	18 total metastases were demonstrated on MRI compared to the 4 on CT. 7 were visualized on the unenhanced MR images, 9 on the scans using gadopentetate dimeglumine, and all 18 on the scans using gadoteridol. Additional lesions were seen on the gadoteridol images in all 4 patients. No adverse events attributable to contrast media occurred. No significant changes in vital signs or laboratory values occurred.	4
25. Dalla-Palma L, Pozzi-Mucelli R. Problematic renal masses in ultrasonography and computed tomography. *Clin Imaging.* 1990;14(2):83-98.	Review/Other-Dx	N/A	Review the use of CT and US in problematic renal masses.	CT is helpful in most of these cases because it enables the evaluation of the calcifications and the density of the fluid content. CT is also helpful in cases of cystic tumors because it shows the enhancement of septae within the masses. Problems with solid masses are the identification of small renal tumors and the definition of the benign or malignant nature of the mass. Although both techniques enable the recognition of most tumors, even if small in diameter, they are still limited in defining the pathological structure of the tumor.	4

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26. Utsunomiya D, Shiraishi S, Imuta M, et al. Added value of SPECT/CT fusion in assessing suspected bone metastasis: comparison with scintigraphy alone and nonfused scintigraphy and CT. *Radiology.* 2006;238(1):264-271.	Observational-Dx	45 patients	To evaluate retrospectively if there is additional diagnostic value of fused single photon emission computed tomographic and CT images in assessing possible bone metastases.	After review of fused images to classify indeterminate lesions, reviewer 1 became more confident in diagnosis of the 15 benign lesions and 2 metastases, and reviewer 2 became more confident in diagnosis of the 7 benign lesions and 1 metastasis. The area under the receiver operating characteristic curve for reviewer 1 was 0.589 for scintigraphic images, 0.831 for separate data sets of scintigraphic and CT images, and 0.947 for fused images. The corresponding areas under the receiver operating characteristic curve for reviewer 2 were 0.771, 0.885, and 0.968, respectively.	3
27. Fuccio C, Ceci F, Castellucci P, et al. Restaging clear cell renal carcinoma with 18F-FDG PET/CT. *Clin Nucl Med.* 2014;39(6):e320-324.	Observational-Dx	69 patients	To assess the usefulness of FDG-PET/CT in the restaging of clear cell RCC patients.	FDG-PET/CT was positive in 42 patients and negative in 27 patients. 16 patients presented single lesions and 26 patients presented multiple localizations of the disease. On a patient basis, 40 patients resulted true positive, 2 patient false positive, 23 patients true negative, and 4 patients false negative. Sensitivity, specificity, accuracy, PPV, and NPV were 90%, 92%, 91%, 95%, and 85%, respectively. On a lesion basis, PET/CT detected 114 areas of abnormal uptake in 42 positive patients of which 112 resulted to be true positive. FDG uptake of the true positive lesions resulted to be high in 83 cases, moderate in 17 lesions, and finally faint in 12 lesions.	3
28. Martinez de Llano SR, Delgado-Bolton RC, Jimenez-Vicioso A, et al. [Meta-analysis of the diagnostic performance of 18F-FDG PET in renal cell carcinoma]. *Rev Esp Med Nucl.* 2007;26(1):19-29.	Meta-analysis	7 studies	To perform a meta-analysis of the literature to evaluate the performance and accuracy of FDG-PET in the detection of primary disease, recurrence and metastasis of RCC.	7 out of 46 studies fulfilled the inclusion criteria and were analyzed. 3 studies evaluated the use of FDG-PET in the differential diagnosis of renal masses. 2 studies analyzed restaging and 2 analyzed the role of FDG-PET in the detection of metastatic disease. All the selected studies were classified according to Flynn's criteria. The authors found the highest sensitivity in restaging with S 0.87 (95% CI, 0.75–0.95) and in metastases detection with sensitivity 0.72 (95% CI, 0.56–0.85) as well as the high specificity in differential diagnosis of renal masses.	M

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29. Park JW, Jo MK, Lee HM. Significance of 18F-fluorodeoxyglucose positron-emission tomography/computed tomography for the postoperative surveillance of advanced renal cell carcinoma. *BJU Int.* 2009;103(5):615-619.	Observational-Dx	63 patients	To evaluate the role of FDG-PET/CT for the surveillance of patients with RCC who have a high risk of local recurrence or distant metastasis, by comparing the results with those of conventional imaging methods.	The FDG-PET/CT accurately classified the presence of a recurrence or metastasis in 56 (89%) patients. FDG-PET/CT had an 89.5% sensitivity, 83.3% specificity, 77.3% PPV, 92.6% NPV, and 85.7% accuracy in detecting recurrence or metastasis, which was not significantly different from the results with conventional methods. Moreover, the accuracy of the FDG-PET/CT by nuclear grade and histological subtypes was not significantly different.	3
30. Wang HY, Ding HJ, Chen JH, et al. Meta-analysis of the diagnostic performance of [18F]FDG-PET and PET/CT in renal cell carcinoma. *Cancer Imaging.* 2012;12:464-474.	Meta-analysis	14 studies	To evaluate whether the integration of CT scans with the PET system could increase the applicability of FDG-PET for RCC.	The pooled sensitivity and specificity of FDG-PET were 62% and 88% respectively, for renal lesions. For detecting extra-renal lesions, the pooled sensitivity and specificity of FDG-PET were 79% and 90%, respectively, based on the scans, and 84% and 91% based on the lesions. The use of a hybrid FDG-PET/CT to detect extra-renal lesions increased the pooled sensitivity and specificity to 91% and 88%, respectively, with good consistency.	M
31. Hillner BE, Siegel BA, Hanna L, Duan F, Quinn B, Shields AF. 18F-fluoride PET used for treatment monitoring of systemic cancer therapy: results from the National Oncologic PET Registry. *J Nucl Med.* 2015;56(2):222-228.	Observational-Dx	2,217 patients who underwent 2,839 scans	To assess the impact of NaF PET results obtained for treatment monitoring of systemic cancer therapy.	The overall rates of prior radionuclide bone imaging were 78%, 76%, and 66% for prostate, breast, and other cancers, respectively. 57% of patients underwent prior NaF PET. Overall change in management associated with NaF PET was 40%. In patients with prior NaF PET scans for comparison, continuing current therapy was planned in 79% when scans showed no change or a decrease or absence of osseous metastasis. Treating physicians planned to switch therapy in 59% of patients after scans showed evidence of new or progressive metastasis. When an additional parameter, estimated prognosis, was worse, switching therapy was even more common (76%).	3

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32. Hillner BE, Siegel BA, Hanna L, et al. Impact of 18F-Fluoride PET on Intended Management of Patients with Cancers Other Than Prostate Cancer: Results from the National Oncologic PET Registry. *J Nucl Med.* 2014;55(7):1054-1061.	Observational-Dx	2,819 nonprostate, compared with 8,284 prostate cancer scans	To report the impact of NaF PET on intended management for patients with other cancer types and compared these results with those in prostate cancer patients.	Overall, NaF PET led to change in intended management in a substantial fraction of nonprostate cancer patients. In the setting of suspected FOM, NaF PET had a lower immediate impact on the treat/nontreat decision in nonprostate vs prostate cancer patients, which is consistent with current practice guidelines.	3
33. Hallscheidt PJ, Bock M, Riedasch G, et al. Diagnostic accuracy of staging renal cell carcinomas using multidetector-row computed tomography and magnetic resonance imaging: a prospective study with histopathologic correlation. *J Comput Assist Tomogr.* 2004;28(3):333-339.	Observational-Dx	82 RCCs	Prospective study to compare accuracy of MDCT and MRI in staging RCC.	MRI achieved accuracy of 78%–87% and CT 80%–83%, which are statistically identical. MRI and CT can be used interchangeably for staging renal cancer.	2
34. Walter C, Kruessell M, Gindele A, Brochhagen HG, Gossmann A, Landwehr P. Imaging of renal lesions: evaluation of fast MRI and helical CT. *Br J Radiol.* 2003;76(910):696-703.	Observational-Dx	29 patients	To compare triphasic helical CT and fast MRI for staging renal cancer.	12/18 renal cancers were correctly staged by CT and MRI. Both MRI and CT are excellent in providing critical staging information, however, CT does so more quickly.	2
35. Goel MC, Mohammadi Y, Sethi AS, Brown JA, Sundaram CP. Pathologic upstaging after laparoscopic radical nephrectomy. *J Endourol.* 2008;22(10):2257-2261.	Observational-Dx	123 patients	Retrospective study of patients undergoing laparoscopic radical nephrectomy to determine the extent of upstaging on histopathology evaluation and correlated the clinical and pathology staging to determine the factors responsible for upstaging.	Pathologic upstaging of malignant renal neoplasms occurred in about 31% of patients following laparoscopic radical nephrectomy. Downstaging was less common and mean tumor size does not significantly change.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. Jeffery NN, Douek N, Guo DY, Patel MI. Discrepancy between radiological and pathological size of renal masses. *BMC Urol.* 2011;11:2.	Observational-Dx	157 patients	To compare the radiological size of solid renal tumors on CT to the pathological size in an Australian population.	Overall, the mean radiological tumor size on CT was 58.3 mm and the mean pathological size was 55.2 mm. On average, CT overestimated pathological size by 3.1 mm (P=0.012). CT overestimated pathological tumor size in 92 (58.6%) patients, underestimated in 44 (28.0%) patients and equaled pathological size in 21 (31.4%) patients. Among the 122 patients with pT1 or pT2 tumors, there was a discrepancy between clinical and pathological staging in 35 (29%) patients. Of these, 21 (17%) patients were downstaged postoperatively and 14 (11.5%) were upstaged. Fuhrman grade correlated positively with radiological tumor size (P=0.039) and pathological tumor stage (P=0.003).	3
37. Liu Y, Song T, Huang Z, Zhang S, Li Y. The accuracy of multidetector Computed Tomography for preoperative staging of renal cell carcinoma. *Int Braz J Urol.* 2012;38(5):627-636.	Observational-Dx	312 patients	To evaluate the accuracy of MDCT in the preoperative staging of RCC.	The difference in tumor size between radiographic and pathological findings was 0.21 cm. In T1a group, the difference was 0.33 cm. Agreement between MDCT and histopathological findings was moderate for T staging (Kappa = 0.469), fair for N staging (Kappa = 0.322), and excellent for M staging (Kappa = 0.932). The sensitivity and specificity of MDCT in detecting perinephric fat invasion were 32.26% and 85.87%, in detecting tumor thrombosis were 84% and 100%, in detecting adrenal gland invasion were 60% and 95.79%, in detecting lymph node involvement were 50% and 96.36%, in detecting distant metastasis were 100% and 99.67%, respectively. In regard to stage grouping, 237/314 patients were correctly staged by MDCT, with an overall accuracy of 75.48%.	3
38. Catalano C, Fraioli F, Laghi A, et al. High-resolution multidetector CT in the preoperative evaluation of patients with renal cell carcinoma. *AJR Am J Roentgenol.* 2003;180(5):1271-1277.	Observational-Dx	40 patients, 2 observers	To determine the accuracy of MDCT using a high resolution technique in preoperative evaluation of patients with RCC.	For Robson stage I of RCC, fat infiltration on 1 mm scans was diagnosed with 96% sensitivity, 93% specificity, and 95% accuracy; PPV of 100% , NPV of 93%. MDCT is an accurate technique.	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Kamel IR, Hochman MG, Keogan MT, et al. Accuracy of breath-hold magnetic resonance imaging in preoperative staging of organ-confined renal cell carcinoma. *J Comput Assist Tomogr.* 2004;28(3):327-332.	Observational-Dx	43 patients (50 lesions)	Retrospective study to determine accuracy of breath-hold MRI for preoperative staging of organ-confined (stage I) RCC.	MRI has accuracy of range 80% and 82% in staging patients with organ-confined RCC, with 90% agreement between readers.	2
40. Roy C, Sr., El Ghali S, Buy X, et al. Significance of the pseudocapsule on MRI of renal neoplasms and its potential application for local staging: a retrospective study. *AJR Am J Roentgenol.* 2005;184(1):113-120.	Observational-Dx	80 tumors	Retrospective study to evaluate the role of MRI in showing a tumoral pseudocapsule to select patients for partial surgery.	MRI findings for isolated analysis of the pseudocapsule for differentiating stage T1/T2 from T3a were sensitivity: 86%, 50%; specificity: 95%, 92%; PPV: 95%, 33%; NPV: 88%, 92%; and accuracy: 93%, 89%, for clear cell and papillary types, respectively. For stage T3a, with both abnormalities of the pseudocapsule and perirenal fat, results were, for overall RCC sensitivity: 84%; specificity: 95%; PPV: 91%; NPV: 91%; and accuracy: 91%. The presence of an intact pseudocapsule is a sign of lack of perinephric fat invasion and predicts that the tumor can be removed by nephron-sparing surgery.	2
41. Hallscheidt P, Wagener N, Gholipour F, et al. Multislice computed tomography in planning nephron-sparing surgery in a prospective study with 76 patients: comparison of radiological and histopathological findings in the infiltration of renal structures. *J Comput Assist Tomogr.* 2006;30(6):869-874.	Experimental-Dx	76 consecutive patients, 2 blinded readers	Prospective study to determine the diagnostic accuracy of MDCT compared to histopathologic findings in tumor staging of RCC, with the focus on tumor stage, vein and artery infiltration, and infiltration of the renal pelvis.	Readers 1 and 2 reached a sensitivity of 1.0 and 1.0 and a specificity of 0.41 and 0.42 for arterial infiltration, a sensitivity of 1.0 and 0.86 and a specificity of 0.58 and 0.5 for venous infiltration, and a sensitivity of 0.75 and 1.0 and a specificity of 0.5 and 0.44 for infiltration of the renal pelvis. The correlation between both readers was 0.7 for all modalities. The multiplanar reconstruction capability of MDCT allowed good sensitivity in predicting arterial infiltration. The lowest specificity was reached in excluding infiltration of the renal pelvis. Despite its high temporal and spatial resolution, the capacity of MDCT to predict intrarenal infiltrations is still limited.	1

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Bonsib SM. The renal sinus is the principal invasive pathway: a prospective study of 100 renal cell carcinomas. *Am J Surg Pathol.* 2004;28(12):1594-1600.	Review/Other-Dx	100 RCCs	To prospectively examine 100 RCCs for renal sinus invasion.	Renal sinus invasion is the most common site of extrarenal extension of renal carcinoma and correlates with tumor type, grade and size. Appropriate evaluation for sinus invasion reduces the incidence of T1b and T2 CC tumors, limiting prognostic utility and suggesting reassessment of the T1 and T2 stage designations.	4
43. Margulis V, Tamboli P, Matin SF, Meisner M, Swanson DA, Wood CG. Redefining pT3 renal cell carcinoma in the modern era: a proposal for a revision of the current TNM primary tumor classification system. *Cancer.* 2007;109(12):2439-2444.	Observational-Dx	419 patients	To evaluate the prognostic significance of venous tumor thrombus and its extent, the presence and location of extrarenal tumor extension, and a combination of both features on survival after the surgical management of patients with pathologic T3 (pT3) RCC.	In multivariate Cox regression analyses, the 2002 AJCC primary tumor classification was not found to be an independent predictor of cancer-specific mortality. A total of 211 patients with extrarenal tumor extension only (50.4%) and 72 patients with venous tumor thrombus only (17.2%) were found to have a similar risk of death from RCC (HR of 1.018; *P*=.957), whereas 136 patients harboring both features (32.5%) were found to be significantly more likely to die from RCC (HR of 2.660; *P*<.001). The authors proposed a new primary tumor classification in which they grouped patients with both ERE and venous tumor thrombus (which was found to be an independent predictor of cancer-specific survival) into a separate staging category, and demonstrated improved prognostic ability when compared with the 2002 AJCC classification (c indexes of 0.625 vs 0.580, respectively).	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Bertini R, Roscigno M, Freschi M, et al. Renal sinus fat invasion in pT3a clear cell renal cell carcinoma affects outcomes of patients without nodal involvement or distant metastases. *J Urol.* 2009;181(5):2027-2032.	Observational-Dx	105 patients with clear RCC	Retrospective study to analyze the impact of sinus fat invasion on cancer specific survival in a cohort of patients with pT3a clear cell RCC.	Median follow-up was 38 months. In the subset of patients with pNx/pN0 M0 (83) the actuarial 5-year cancer specific survival was 71.9% and 45.5% for those with perinephric fat invasion only and sinus fat invasion, respectively (P=0.025). Sinus fat invasion achieved an independent predictive role on multivariable Cox regression analysis (P=0.048, HR 2.06). Sinus fat invasion in clear cell RCC significantly affects cancer specific survival in patients without nodal or distant metastases. However, sinus fat invasion is not associated with worse cancer specific survival in cases of metastatic disease.	2
45. Thompson RH, Leibovich BC, Cheville JC, et al. Is renal sinus fat invasion the same as perinephric fat invasion for pT3a renal cell carcinoma? *J Urol.* 2005;174(4 Pt 1):1218-1221.	Observational-Dx	205 patients	To evaluate the prognostic importance of renal sinus vs perinephric fat invasion in a large series of patients with pT3a disease.	Patients with renal sinus fat invasion were 63% more likely to die of RCC compared with those with perinephric fat invasion (RR 1.63, 95% CI, 1.09–2.46, P=0.018). In addition, the risk of death persisted in multivariate analysis after adjusting for regional lymph nodes and distant metastases (RR 1.91, 95% CI, 1.26–2.89, P=0.002) and after adjusting for the Mayo Clinic SSIGN (stage, size, grade and necrosis) score (RR 1.90, 95% CI, 1.25–2.88, P=0.003). Results indicate that clear cell tumors invading the renal sinus fat are more aggressive than tumors with perinephric fat involvement.	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Margulis V, Tamboli P, Matin SF, Meisner M, Swanson DA, Wood CG. Location of extrarenal tumor extension does not impact survival of patients with pT3a renal cell carcinoma. *J Urol.* 2007;178(5):1878-1882.	Observational-Dx	365 patients	Evaluate the prognostic significance of location of extrarenal tumor extension on cancer specific survival following surgery to assess and improve the predictive ability of the current pT3a primary tumor classification.	No difference in 5-year cancer specific survival between 166 patients (45.5%) with sinus fat invasion and 199 (54.5%) with perinephric fat invasion only (50.8% and 54.1%, *P*=0.782 respectively). On univariate analyses neither sinus fat invasion nor the location of extrarenal extension, assessed as perinephric fat vs sinus fat vs perinephric plus sinus fat, correlated with cancer specific survival following surgical treatment (HR 1.052, *P*=0.783 and HR 1.072, *P*=0.543, respectively). After adjusting for the effects of nodal and systemic metastases tumor grade and sarcomatoid differentiation remained independent predictors of RCC specific survival.	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Sidana A, Donovan JF, Gaitonde K. Surgeons' preferences and practice patterns regarding intraoperative frozen section during partial nephrectomy. *Urol Oncol.* 2014;32(6):864-868.	Review/Other-Dx	197 responses	A survey was performed to evaulate the preferences and practice patterns of urologists regarding intraoperative frozen section during partial nephrectomy.	A total of 197 responses were received. Overall, 69% and 58% of respondents chose to obtain frozen section (always or sometimes) during open partial nephrectomy and laparoscopic partial nephrectomy, respectively. There was a strong correlation between the surgeons' preferences during open partial nephrectomy and laparoscopic partial nephrectomy. Younger surgeons are less likely to obtain frozen section during open partial nephrectomy. For surgeons who did not routinely obtain frozen section "confidence about complete resection" was the most common reason (79%), followed by "no change in management with positive margins" (35%). Most surgeons (75%) believed the margins to be negative, if surgical margin was free of tumor microscopically by a single cell layer. Older surgeons considered negative margins to be free of tumor microscopically by ≥5 mm. Overall, 54% and 42% of respondents would repeat frozen section for positive microscopic margins during open partial nephrectomy and laparoscopic partial nephrectomy, respectively. Of the respondents, 95% would not recommend additional treatment for positive margins on final pathology.	4
48. Sawai Y, Kinouchi T, Mano M, et al. Ipsilateral adrenal involvement from renal cell carcinoma: retrospective study of the predictive value of computed tomography. *Urology.* 2002;59(1):28-31.	Observational-Dx	73 patients	Retrospective analysis to assess the value of CT in detecting ipsilateral adrenal involvement by RCC.	CT had 100% sensitivity, 76% specificity, 11% PPV, and 100% NPV for ipsilateral adrenal involvement of RCC. Normal adrenal images on CT could exclude adrenal involvement by RCC, but radical nephrectomy should be performed in patients with large tumors.	2

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Ficarra V, Galfano A, Guille F, et al. A new staging system for locally advanced (pT3-4) renal cell carcinoma: a multicenter European study including 2,000 patients. *J Urol.* 2007;178(2):418-424; discussion 423-414.	Observational-Dx	1,969 patients	Multicenter study. Clinical and pathological data on a large series of patients undergoing radical nephrectomy was analyzed to provide an adequate prognostic stratification for locally advanced RCC and propose a new TNM classification.	5-year cancer specific survival was 60% for pT3a, 46.2% for pT3b, 10% for pT3c and 12% for pT4 tumors (P<0.0001). According to median survival 3 prognostic groups were identified, including 1) patients with renal vein thrombosis (117 months), fat invasion (98 months) or infradiaphragmatic vena caval thrombosis (67 months), 2) patients with adrenal invasion alone (24 months), renal vein thrombosis plus fat invasion (24 months) or infradiaphragmatic vena cava plus fat invasion (24 months) and 3) patients with renal or infradiaphragmatic caval thrombosis plus adrenal involvement (11 months), supradiaphragmatic vena caval thrombosis (12 months) or Gerota's fascia invasion (12 months). 5-year cancer specific survival rates in groups 1 to 3 were 61%, 35% and 12.9%, respectively (P<0.0001).	2
50. Moch H, Artibani W, Delahunt B, et al. Reassessing the current UICC/AJCC TNM staging for renal cell carcinoma. *Eur Urol.* 2009;56(4):636-643.	Review/Other-Dx	62 articles	Review article with focus on reassessing the current TNM staging system for RCC.	Special emphasis should be put on renal sinus invasion for stage evaluation. Retrospective studies relying on material collected at a time when no emphasis was placed on adequate sampling of the renal sinus should be treated with caution. In view of new treatment opportunities, the current TNM staging system of RCC and any other staging system must be dynamic.	4
51. Moinzadeh A, Libertino JA. Prognostic significance of tumor thrombus level in patients with renal cell carcinoma and venous tumor thrombus extension. Is all T3b the same? *J Urol.* 2004;171(2 Pt 1):598-601.	Observational-Dx	153 patients	To examine the prognostic significance of venous tumor thrombus extension in patients with RCC with particular emphasis on whether the level of thrombus in the IVC impact long-term survival and if there is a difference in long-term survival when tumor thrombus is in the renal vein vs the IVC for patients classified as T3b by 1997 TNM staging.	Overall 10-year cancer specific survival for patients was 30%, 19% and 29% for level I, II and III, respectively. Patient survival at 5 and 10 years was not significantly different between the 3 IVC levels (P=0.48). Ten-year survival of patients with renal vein involvement (66%) vs level I (29%) was significantly different (P=0.0001). The level of tumor thrombus in the IVC does not significantly effect long-term survival. Ten-year survival of patients classified as T3b is statistically different for patients having tumor thrombus in the renal vein compared to level I.	2

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Kim HL, Zisman A, Han KR, Figlin RA, Belldegrun AS. Prognostic significance of venous thrombus in renal cell carcinoma. Are renal vein and inferior vena cava involvement different? *J Urol.* 2004;171(2 Pt 1):588-591.	Observational-Dx	226 patients had nephrectomy and tumor thrombectomy, 654 patients undergoing nephrectomy without venous involvement	To examine the prognostic significance of venous thrombus in RCC. Records of patients who had a nephrectomy and tumor thrombectomy were reviewed and compared to those of patients undergoing nephrectomy without venous involvement.	For patients with pT3b disease, local tumor stage and grade are better predictors of prognosis than extent of venous involvement. Authors support the current TNM classification of venous involvement with renal vein and IVC invasion categorized as T3b and IVC involvement above the diaphragm categorized as T3c.	3
53. Hallscheidt PJ, Fink C, Haferkamp A, et al. Preoperative staging of renal cell carcinoma with inferior vena cava thrombus using multidetector CT and MRI: prospective study with histopathological correlation. *J Comput Assist Tomogr.* 2005;29(1):64-68.	Experimental-Dx	23 patients	Prospective study to evaluate the accuracy of MDCT and MRI in staging RCC with caval thrombus.	CT thrombus detection sensitivity and specificity for both readers was 0.93 and 0.8 respectively. MRI sensitivity and specificity for both readers was 1.0/0.85 and 0.75. CT and MRI accuracy was 78% and 72%, 88% and 76% respectively.	2
54. Ergen FB, Hussain HK, Caoili EM, et al. MRI for preoperative staging of renal cell carcinoma using the 1997 TNM classification: comparison with surgical and pathologic staging. *AJR Am J Roentgenol.* 2004;182(1):217-225.	Observational-Dx	MRI in 40 consecutive patients with 42 RCCs before radical (n=35) or partial (n=4) nephrectomy or exploratory laparotomy (n=3)	Retrospective review to determine accuracy of MRI for preoperative staging of RCC using the 1997 TNM classification.	Agreement between MRI and surgical-pathologic staging was good for T staging (kappa = 0.72 and 0.78 for reviewers 1 and 2 respectively), poor for N staging (kappa = 0.13, both reviewers), good for M staging (kappa = 0.66, both reviewers), and excellent for the assessment of venous involvement (kappa = 0.93, both reviewers). MRI is reliable, in particular assessing venous involvement.	3
55. Aslam Sohaib SA, Teh J, Nargund VH, Lumley JS, Hendry WF, Reznek RH. Assessment of tumor invasion of the vena caval wall in renal cell carcinoma cases by magnetic resonance imaging. *J Urol.* 2002;167(3):1271-1275.	Observational-Dx	12 patients	To evaluate the role of MRI in patients with renal cancer and inferior vena caval involvement with reference to its ability to characterize the extent and nature of inferior vena caval tumor extension and wall invasion.	On MRI the extent and nature of the inferior vena caval tumor was correctly defined in all cases. The sensitivity, specificity and accuracy of inferior vena caval wall invasion were 100%, 89% and 92%, respectively.	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Zini L, Destrieux-Garnier L, Leroy X, et al. Renal vein ostium wall invasion of renal cell carcinoma with an inferior vena cava tumor thrombus: prediction by renal and vena caval vein diameters and prognostic significance. *J Urol.* 2008;179(2):450-454; discussion 454.	Observational-Dx	446 patients	To determine whether renal vein ostium wall invasion could be predicted by renal vein and IVC diameter on imaging. To also determine whether it is a prognostic factor for recurrence and survival after radical nephrectomy and thrombus ablation for RCC with an IVC tumor thrombus.	Renal vein ostium wall invasion was present in 13/32 patients (40.6%). It significantly correlated with mean +/- SD IVC anteroposterior diameter (27.8 +/- 10.2 vs 17.3 +/- 6.8 mm, *P*=0.01) and with the largest mean renal vein ostium diameter (22.3 +/- 7.9 vs 12.6 +/- 6.9 mm, *P*=0.01). The upper level of the IVC thrombus correlated with renal vein ostium invasion (*P*=0.002). The IVC anteroposterior diameter or renal vein ostium diameter cutoff value to predict wall invasion with 90% sensitivity was 18 and 14 mm, respectively. The AUC was 0.78 for IVC diameter and 0.86 for renal vein ostium diameter. No IVC recurrence was observed. Renal vein ostium wall invasion was associated with a higher risk of recurrence and decreased specific survival (*P*=0.01 and 0.03, respectively). The association of ostium renal vein wall invasion with death from RCC was seen on multivariate analysis after adjusting for tumor size, TNM stage and thrombus level (RR 5.9, 95% CI, 1.45–30.8, *P*=0.01).	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Rodriguez Carvajal R, Orgaz A, Leal JI, et al. Renal embolization and nephrectomy in a single surgical act in high-risk renal tumor pathology. *Ann Vasc Surg.* 2011;25(2):222-228.	Review/Other-Tx	7 patients	To describes the experience and results obtained with renal embolization concomitant with, and also with variations in the embolization technique that offer significant advantages over conventional embolization techniques.	In all the cases, 100% technical success was obtained with the embolization and nephrectomy. The mean duration of surgery in the case of embolization with coils was 45 minutes, and 25 minutes in the case of embolization with Amplatzer. A mean volume of 115 mL of contrast medium was used in the case of embolization with coils, whereas for the other cases, a mean volume of 71 mL of iodinated contrast was used. Among all the patients, only 2 of them required to be cared at the intensive care unit during 24 hours. On an average, reported blood loss was 380 mL. During the procedure, 2 patients (28.6%) required a transfusion of 2 units of red cells. No cases of perioperative or postoperative mortality were reported. With respect to morbidity, only 1 patient (14.3%) experienced a complication in the form of a superficial infection of the surgical wound, which was later resolved by antibiotic therapy. One patient (14.3%) presented a slightly higher preintervention level of creatinine (1.42). Two patients (28.6%), both of whom underwent embolization by using coils, experienced deterioration of postoperative renal function.	4
58. Munro NP, Woodhams S, Nawrocki JD, Fletcher MS, Thomas PJ. The role of transarterial embolization in the treatment of renal cell carcinoma. *BJU Int.* 2003;92(3):240-244.	Review/Other-Dx	25 patients	Retrospective analysis of the role of transarterial renal embolization in the treatment of RCC.	Transarterial embolization is associated with minimal morbidity and complications, and subsequent symptom control is good. The effect of palliative embolization on RCC progression is unknown.	4
59. Fielding JR, Aliabadi N, Renshaw AA, Silverman SG. Staging of 119 patients with renal cell carcinoma: the yield and cost-effectiveness of pelvic CT. *AJR Am J Roentgenol.* 1999;172(1):23-25.	Review/Other-Dx	119 patients	Computerized review of medical records to determine the yield and cost-effectiveness of pelvic CT in staging RCC.	Total estimated cost of the 119 CT examinations of the pelvis was $40,698 ($342 each). No findings of probable malignancy were identified. In 27 patients, CT showed benign findings; these results did not cause planned surgery to be delayed. Three of these 27 patients underwent further radiologic tests at an estimated total cost of $243.	4

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
60. Khaitan A, Gupta NP, Hemal AK, Dogra PN, Seth A, Aron M. Is there a need for pelvic CT scan in cases of renal cell carcinoma? *Int Urol Nephrol.* 2002;33(1):13-15.	Review/Other-Dx	400 patients	Retrospective study to determine the necessity of pelvic CT in patients of RCC.	Of the 400 cases, 114 were stage I, 68 were stage II, 99 were stage III and 119 were stage IV. In all patients, tumor was identified in the kidney on preoperative CT scan. 14 patients (3.5%) had an abnormality on pelvic CT. Five (1.25%) had category 1, 3 (0.75%) had category 2 and 6 (1.5%) had category 3 abnormality on pelvic CT. However, all these abnormalities in pelvis were detected prior to CT by other investigations (US or plain radiograph). Of the 6 cases with malignant findings, 2 had superficial bladder cancer, 1 had RCC in a pelvic kidney and 3 had bone metastases in the pelvis. Pelvic CT does not offer additional information in the vast majority of cases with RCC and should be performed selectively. Thus the cost of diagnostic imaging in RCC can be reduced.	4
61. Heidenreich A, Ravery V. Preoperative imaging in renal cell cancer. *World J Urol.* 2004;22(5):307-315.	Review/Other-Dx	N/A	To review the current status of preoperative imaging modalities in RCC.	CT remains the most appropriate imaging modality to differentiate benign from malignant lesions.	4
62. Guimaraes AR, Tabatabei S, Dahl D, McDougal WS, Weissleder R, Harisinghani MG. Pilot study evaluating use of lymphotrophic nanoparticle-enhanced magnetic resonance imaging for assessing lymph nodes in renal cell cancer. *Urology.* 2008;71(4):708-712.	Observational-Dx	9 patients	To assess lymphotrophic nanoparticle-enhanced MRI in identifying malignant nodal involvement in patients with renal neoplasms.	Lymphotrophic nanoparticle-enhanced MRI had high sensitivity (100%) and specificity (95.7%) in renal neoplasms.	3
63. Hsu RM, Chan DY, Siegelman SS. Small renal cell carcinomas: correlation of size with tumor stage, nuclear grade, and histologic subtype. *AJR Am J Roentgenol.* 2004;182(3):551-557.	Observational-Dx	213 consecutive RCCs	Retrospective review to correlate size of RCC with tumor stage, nuclear grade, and histologic subtype in patients treated using partial or radical nephrectomy.	Of 50 lesions ≤3 cm 38% were T3a, and 28% were high grade (Fuhrman 3, 4). Lesions <5 cm had the same T-stage.	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Santini D, Procopio G, Porta C, et al. Natural history of malignant bone disease in renal cancer: final results of an Italian bone metastasis survey. *PLoS One.* 2013;8(12):e83026.	Observational-Tx	398 patients	To report final data from a large Italian multicenter study of patients with bone metastasis from RCC.	Median time to bone metastasis was 25 months for patients without bone metastasis at diagnosis. Median time to diagnosis of bone metastasis by MSKCC risk was 24 months for good, 5 months for intermediate, and 0 months for poor risk. Median number of skeletal-related events/patient was 1, and 71% of patients experienced at least 1 skeletal-related event. Median times to first, second, and third skeletal-related event were 2, 5, and 12 months, respectively. Median survival was 12 months after bone metastasis diagnosis and 10 months after first skeletal-related event. Among 181 patients who received zoledronic acid, median time to first skeletal-related event was significantly prolonged vs control (n = 186) (3 months vs 1 month for control; $P<0.05$).	2
65. Shuch B, La Rochelle JC, Klatte T, et al. Brain metastasis from renal cell carcinoma: presentation, recurrence, and survival. *Cancer.* 2008;113(7):1641-1648.	Review/Other-Tx	138 patients	The outcome of patients with RCC brain metastases was reviewed at a single RCC referral center to assist with the formulation of management guidelines.	A total of 138 patients were identified with RCC brain metastases, of whom 92% had clear cell RCC and 95% had synchronous extracranial metastases. Central nervous system symptoms were noted in 67% of patients. Symptomatic central nervous system tumors were larger (2.1 cm vs 1.3 cm; $P<.001$) and more frequently required a craniotomy ($P<.001$). The median overall survival after a diagnosis of RCC brain metastases was 10.7 months; the 1-year, 2-year, and 5-year survival rates were 48%, 30%, and 12%, respectively. Median central nervous system recurrence was 9 months after RCC brain metastases treatment. The initial number of tumors (>1 tumor) was found to be an independent predictor of central nervous system recurrence (HR of 3.72; $P<.001$). Those patients with 1 and >1 lesion had a median central nervous system RFS of 13 months and 4 months, respectively ($P<.001$). Patients receiving interleukin-2 after central nervous system treatment had a response rate of 17%.	4

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Ozulker T, Ozulker F, Ozbek E, Ozpacaci T. A prospective diagnostic accuracy study of F-18 fluorodeoxyglucose-positron emission tomography/computed tomography in the evaluation of indeterminate renal masses. *Nucl Med Commun.* 2011;32(4):265-272.	Observational-Dx	15 patients	To evaluate the efficacy of FDG-PET/CT in the detection of RCC in patients with indeterminate renal masses.	15 patients had RCC (14 clear-cell RCC, 1 papillary RCC). 3 renal tumors were benign, corresponding to 2 renal cortical cysts and 1 oncocytoma. FDG-PET/CT accurately detected 7 malignant lesions and yielded false-negative results in 8 patients. FDG-PET/CT was true negative in 2 patients with a renal cortical cyst and false positive in a patient with oncocytoma. PET showed a sensitivity of 46.6%, specificity of 66.6%, and accuracy of 50% for primary RCC tumors. The median size of visualized tumors was greater than the median size of nonvisualized tumors, and the average Fuhrman grade of the patients with FDG-positive malignant lesions were higher than that of the patients with FDG-negative lesions. In malignant tumors, the change between early and delayed imaging for average standardized uptake values and maximum standardized uptake values were not statistically significant.	3
67. Kang DE, White RL, Jr., Zuger JH, Sasser HC, Teigland CM. Clinical use of fluorodeoxyglucose F 18 positron emission tomography for detection of renal cell carcinoma. *J Urol.* 2004;171(5):1806-1809.	Observational-Dx	66 patients had 90 PET scans	Retrospective review to evaluate role of FDG-PET in patients with RCC. Accuracies of PET, chest CT, abdominal/pelvic CT and bone scan were compared.	For primary tumors, PET had sensitivity of 60% and specificity of 100%, CT had sensitivity of 91.7% and specificity of 100%. For lymph node metastases PET had sensitivity of 75% and specificity of 100%. CT had sensitivity of 92.6% and specificity of 98.1%. For metastases to the lung parenchyma, PET had sensitivity of 75% and specificity of 97% compared to 91.1% and 73.1%, respectively, for chest CT. For bone metastases, PET had sensitivity of 77.3% and specificity of 100.0%, compared to 93.8% and 87.2% for combined CT and bone scan. PET may have a complementary role as a problem solving tool in cases that are equivocal.	3

Renal Cell Carcinoma Staging
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Majhail NS, Urbain JL, Albani JM, et al. F-18 fluorodeoxyglucose positron emission tomography in the evaluation of distant metastases from renal cell carcinoma. *J Clin Oncol.* 2003;21(21):3995-4000.	Observational-Dx	24 patients	To evaluate role of FDG-PET in detection of distant metastases from RCC.	FDG-PET performance in detecting 33 pathologically-proven metastases in 21 patients: 64% sensitivity, 100% specificity, and 100% PPV. False negatives: 7 lung, 1 adrenal, 1 chest wall, 1 brain, and 2 mediastinum nodal metastases. FDG-PET is not a sensitive imaging modality for the evaluation of metastatic RCC and may not adequately characterize small metastatic lesions. However, positive FDG-PET is predictive for the presence of RCC in lesions imaged, may complement anatomic radiologic imaging modalities, and may alleviate the need for a biopsy in selected situations. A negative FDG-PET, however does not rule out active malignancy.	3

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

CI = Confidence interval

CT = Computed tomography

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

HR = Hazard ratio

IVC = Inferior vena cava

MDCT = Multidetector computed tomography

MRI = Magnetic resonance imaging

NaF = 18-F-sodium fluoride

NPV = Negative predictive value

PET = Positron emission tomography

PPV = Positive predictive value

RCC = Renal cell carcinoma

RFS = Recurrence-free survival

RR = Relative risk

US = Ultrasound