Open Partial Nephrectomy

13

Patrick A. Kenney, Matthew F. Wszolek,
and John A. Libertino

Introduction

Despite broader acceptance of active surveillance and ablative approaches, surgical excision remains the standard of care for locally confined renal cell carcinoma (RCC). Historically, radical nephrectomy (RN) has been utilized to treat locally confined RCC, regardless of tumor size and complexity. RN remains overutilized for RCC amenable to partial nephrectomy (PN) despite contemporary studies demonstrating equivocal oncologic outcomes between PN and RN for T1 RCC. Comparable oncologic outcomes coupled with contemporary studies correlating RN with increased cardiovascular morbidity, development of chronic kidney disease (CKD), and inferior overall survival have led to more widespread acceptance of nephron-sparing surgery (NSS). To this end, the 2009 American Urologic Association and 2010 European Association of Urology guidelines recommend PN for T1 RCC when technically feasible especially when there is a need to preserve renal function [1, 2].

P.A. Kenney (✉) • M.F. Wszolek
Department of Urology, MD Anderson Cancer Center, Houston, TX, USA

J.A. Libertino, M.D. (✉)
Institute of Urology, Lahey Clinic, 41 Mall Road, Burlington, MD 01805, USA
e-mail: John.A.Libertino@Lahey.org

PN however remains a challenging endeavor requiring complete tumor resection with a negative margin and maximal preservation of functioning renal parenchyma. The chief advantages of PN compared to RN include avoiding the overtreatment of benign renal masses without compromising oncologic efficacy in malignant tumors and preserving renal function to minimize postoperative CKD, morbidity, and mortality. This chapter will provide a detailed discussion of the rationale for PN as well as its current indications. The importance of minimizing renal ischemia and other predictors of postoperative CKD will be discussed. The techniques of open PN will be described as will perioperative management. Minimally invasive approaches, ablative therapies, and active surveillance will be discussed in other chapters.

Historical Perspective

In 1887 Vincenz Czerny (1842–1915) performed the first planned PN for a renal tumor (angiosarcoma) over 15 years after Gustav Simon (1824–1876), his predecessor at Heidelberg, Germany, performed both the first planned nephrectomy and PN for nonmalignant renal pathology [3]. Initial interest in PN, however, weaned due to concerns about complications including intraoperative hemorrhage, delayed bleeding, and urinary fistulae [4]. The observation that a patient could survive with one functioning kidney after nephrectomy also

J.A. Libertino (ed.), *Renal Cancer: Contemporary Management*,
DOI 10.1007/978-1-4614-7236-0_13,

diminished early interest in NSS [3]. In the early twentieth century, nephrectomy was considered a standard therapy for malignant renal tumors due to the technical challenges associated with advanced clinical stage at presentation and concerns about perinephric tumor extension, although PN was occasionally employed in the treatment of benign conditions such as cysts, infarcts, caruncles, calculi, or localized hydronephrosis [3]. In the late twentieth century, the necessity of radical Halstedian resections for renal cancer was questioned by pathologic studies demonstrating the non-invading, expansile local growth of renal tumors [3] as well as studies reporting a low rate of metastasis from small renal tumors [5]. In 1950 Vermooten notably questioned the necessity of RN in all cases of RCC, even in the presence of a functioning contralateral kidney, and established the basis for the modern approach of NSS for RCC [6]. For the next several decades, however, PN was rarely performed even in patients with solitary kidneys, renal dysfunction, or bilateral tumors [7]. As researched by Herr, surgical textbooks written between 1937 and 1970 do not mention PN for renal cancer [3]. Surgical advancements in the 1960s and 1970s, more specifically renal hypothermia and resection techniques based on segmental blood supply which permitted resection and reconstruction in a bloodless field, as well as published favorable local recurrence rates (4–10 %) and survival rates comparable to RN in patients with solitary kidneys and bilateral tumors perked interest in the widespread use of PN in RCC [3, 8].

In the late 1970s and 1980s, progressive urologists increasingly questioned the rationale of removing an entire kidney for a small renal mass leading to the modern era of routine elective PN. As mentioned previously, the concept was not novel. However, advancements in technique and anatomical knowledge, promising local recurrence rates and survival outcomes in preliminary studies of essential PN, and a downward stage migration resulting from more frequent axial imaging provided the foundation for the preliminary experiences of elective PN for RCC patients with normal contralateral renal function. As often true of any dramatic paradigm shift, the change was not immediate or unanimous. Opponents raised concerns over inadequate excision of the primary tumor and possible occult tumor in the renal remnant. Licht and Novick in 1993 published their short-term experience of 241 PNs in patients with a normal contralateral kidney. They reported a <1 % local recurrence rate and 95 % survival rate [9]. Subsequent publications with longer follow-up validated these results and solidified the role of PN in the treatment of small renal masses with a normal contralateral kidney [10, 11]. With continued technical advancements including intraoperative ultrasound and more effective hemostatic agents, urologists have recently expanded indications for NSS to include larger tumor size, multiple tumors in a single operation, and complex locations such as hilar, endophytic, and centrally located lesions. Recently, the role of NSS has been further solidified by the observation that RN compared to PN is associated with an increased risk of CKD and non-cancer-related morbidity and mortality [12, 13]. Currently, urologists are focused on techniques to minimize ischemic injury and also lessen surgical morbidity by minimally invasive approaches.

Epidemiology of Small Renal Masses

Kidney cancer is the 13th most common malignancy worldwide with 270,000 new cases in 2008 [14]. In the United States, there will be an estimated 64,770 new cases and 13,570 deaths from renal tumors (including RCC and urothelial renal pelvis tumors) in 2012 [15]. For cases with pathologic confirmation in the US Surveillance Epidemiology, and End Results (SEER) database, over 90 % of "renal tumors" were RCC, while the majority of the remaining tumors were urothelial tumors of the renal pelvis [16]. For malignant renal tumors, the clear cell (conventional) type constitutes approximately 70 % of cases with papillary, chromophobe, renal medullary, and collecting duct comprising the remaining cases [17]. Established risk factors for RCC

include increasing age [16, 18], male sex [14], geographic location (higher in the USA and Europe) [19], race (lower in Asian/Pacific descendent in the USA) [16, 18], smoking [20], obesity [21–23], and hypertension [21].

Total kidney cancer incidence increased for an approximately 20-year period from the 1970s to the 1990s, but has plateaued or declined recently in many countries worldwide [19, 24]. In the United States, where histologic information is available unlike many other cancer registries, the rates of renal pelvis urothelial tumors have declined, while RCC rates have continued to rise among all age classifications, tumor sizes, and racial groups [18]. The increased incidence of RCC has been attributed to the incidental diagnosis of small, asymptomatic renal masses due to more frequent usage of axial imaging. Contemporary studies support this observation. A study from the US National Cancer Data Base between 1993 and 2004 showed a significant increase in Stage I RCC with a corresponding decrease in Stage II–IV RCC [25]. Further, the mean size of Stage I RCC decreased from 4.1 in 1993 to 3.6 cm in 2003 with a particular increase in incidence of tumors <3 cm [25, 26]. Stage migration may account for the recent plateauing of RCC mortality rates in Europe [24] and the USA [16, 18]. However, other factors are likely also contributing to this trend as the survival of RCC patients with more advanced disease has improved recently as well. Possible explanations include early detection of all stages through incidental diagnosis and recent therapeutic advancements including targeted therapy [16, 18].

There is a distinct relationship between tumor size and risk of malignancy. Smaller lesions are more likely to be benign tumors such as oncocytoma, angiomyolipoma, papillary adenoma, and metanephric adenoma. In the Mayo Clinic experience, 6.3 % of tumors greater than 7 cm were benign compared to 46.3 % of tumors less than 1 cm [27]. Further larger tumor size is associated with an increased risk of high-grade compared to low-grade RCC and clear cell compared to papillary RCC [27]. For renal masses less than 4 cm treated surgically, upstaging to T3 and advanced grade was both associated with increasing tumor size, especially for tumor greater than 3 cm [28, 29]. The relationship between tumor size and risk of metastasis at presentation has been established. Patients with tumor 1 cm or less, 1.1–2 cm, 2.1–3 cm, and 3.1–4 cm had prevalence of metastasis at diagnosis of 1.4 %, 2.5 %, 4.7 %, and 7.4 %, respectively, in a recent SEER study[30]. The most rapid increase in both the prevalence of metastases at diagnosis and disease-specific death occurred for tumor sizes between 4 and 12 cm [30]. A similar pattern to the increased risk of metastasis at presentation with tumors >3 cm is evident in the probability of de novo asynchronous metastatic RCC in postsurgical treated patients [31].

Oncologic Efficacy of Partial Nephrectomy

Traditionally, RN has been the treatment of choice for renal cortical tumors. PN was performed only in "essential" cases such as patients with solitary kidneys, bilateral renal tumors, or severe chronic renal insufficiency in order to avoid dialysis dependence. Consistent with trends across other surgical disciplines favoring organ preservation, the American Urologic Association [1] and European Association of Urology [2] have recommended PN as a treatment for T1 (<7 cm) RCC in patients with two functioning kidneys. The rationale driving this paradigm shift was multifactorial including concerns over the relationship between CKD- and non-RCC-related mortality and a downward stage migration in RCC resulting in an increased detection of renal cortical tumor amenable to PN. Since the goal of any oncologic procedure is local cancer control, the aforementioned factors would be irrelevant if PN was inferior to RN in oncologic outcomes.

There is significant selection bias in early retrospective studies comparing the oncologic efficacy of PN versus RN as many of the PNs were performed in "essential" cases. A group from Mayo Clinic reported a case-control study comparing PN to RN in elective cases with unilateral RCC with a normal contralateral kidney. Each group contained 164 patients and was matched for tumor size, pathologic stage (97 % T1), grade, age, sex, and year of surgery.

Table 13.1 TNM staging of renal cancer [109]

T1: Tumor <7 cm in greatest dimension, confined to kidney
T1a: Tumor <4 cm, confined to kidney
T1b: Tumor between 4-7 cm, confined to kidney
T2: Tumor >7 cm in greatest diameter, confined to kidney
T2: Tumor >7 cm in greatest diameter, confined to kidney
T2a: Tumor >7 cm but ≤ 10 cm, confined to kidney
T2b: Tumor >10 cm, confined to kidney
T3: Tumor extends into major veins or perinephric tissues but not into ipsilateral adrenal gland or beyond Gerota fascia
T3a: Tumor grossly extends into the renal vein or its segmental branches, or tumor invades perirenal and/or renal sinus fat
T3b: Tumor grossly extends into the vena cava below the diaphragm
T3c: Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4 : Tumor invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)
N: Regional lymph nodes
NX: Regional lymph nodes cannot be assessed
N0: No lymph node metastasis
N1: Metastasis in regional lymph nodes
M: Distant metastases
MX: Metastases cannot be assessed
MO: No distant metastases
M1: Distant metastases

There was no difference in oncologic outcomes as 10-year cancer-specific survival (96 % RN vs. 98 % PN) and metastasis-free survival (95 % RN vs. 98 % PN) were similar between the two groups. There was no difference in 10-year overall survival as well (74 % RN vs. 73 % PN) [32].

The EORTC Intergroup (EORTC 30904) conducted a non-inferiority Phase III trial comparing PN and RN for <5 cm solitary tumors suspicious for RCC in patients with normal contralateral kidneys. Prior to discussing the results, the study's shortcomings should be addressed. Foremost, the analysis was underpowered due to poor accrual (541 patients enrolled with 1,300 patients required) and there was a >10 % crossover rate following randomization. Also, the small number of total deaths (117) and cancer-related deaths [12] limited meaningful comparative statistics relating to survival. In the intent to treat analysis, unexpectedly, RN had superior overall survival compared to the PN (81.1 % vs. 75.7 %, $p=0.03$). In secondary analysis of RCC patients only, and clinically and pathologically eligible patients, the trend in overall survival was no longer statistically significant. The estimated risk of RCC-related death and 10-year progression rates (3.3 % after RN and 4.1 % after PN, $p=0.48$) were similar between the two groups. Since only 3 % of the PN patients died from RCC, this study supports the oncologic efficacy of NSS for T1 disease [33].

The remainder of this section will detail pertinent literature relating to the oncologic efficacy of PN compared to RN based on primary tumor stage (Table 13.1). Table 13.2 summarizes many of the studies reporting oncologic outcomes in T1 RCC.

T1a Tumors

A competing-risk population-based SEER analysis comparing oncologic outcomes after PN ($n=1,622$) versus RN ($n=5,658$) for T1aN0M0 was recently published. There was no difference in the 5-year cancer-specific mortality rate after adjusting for other cause mortality (1.8 % for PN vs. 2.5 % for RN, $p=0.5$) [34]. An international multi-institutional retrospective analysis of T1a also showed no difference in the rate of cancer-specific deaths (2.2 % vs. 2.6 %, $p=0.8$) or local recurrence (0.8 % vs. 0.6 %, $p=0.6$) after PN ($n=314$) compared to RN ($n=499$) [35]. Single-institution studies have published comparable 5-year disease-specific survival (95–96.1 %) and local recurrence rates (0–0.9 %) [36, 37].

Table 13.2 Oncologic outcomes of open PN for T1 TCC (NR – not reported) [34–37, 39–41, 110]

	Study	# of patients	Follow-up (months)	Local recurrence	Five-year disease-specific survival
T1a	Crepel et al.	1,622	24	NR	98.2 %
	Patard et al.	314	51	0.8 %	97.8 %
	Antonelli et al.	176	59	0.6 %	96.1 %
	Lee at al.	79	40	0	95.0 %
T1b	Crepel et al.	275	40	NR	93.8 %
	Patard et al.	65	51	3.6 %	97.8 %
	Weight et al.	212	49	NR	93.0 %
	Antonelli et al.	52	54	1.9 %	99.0 %
	Joniau et al.	67	40	4 %	95.8 %
	Pahernik et al.	102	56	1.7 %	

Table 13.3 Oncologic outcomes of open PN for > T1 RCC [42, 43, 111]

Study	Number of patients per pathologic stage	% elective	Follow-up (months)	Local recurrence	Disease-specific survival
Margulis et al.	T2 – 8 T3a – 22 T3b – 4	27 %	62	0 %	78 %
Breau et al.	T2 – 32 T3a – 28 T3b – 9	42 %	38	6 %	83 %
Karellas et al.	T2 – 34 T3a – 0 T3b – 0	86 %	17	NR	89 %

T1b Tumors

A recent SEER population-based analysis of T1bN0M0 RCC compared matched PN (n=275) and RN (n=1,100) groups. In regression models controlling for age, tumor size, and year of surgery, there was no difference in 5-year cancer-specific survival between PN and RN (91.4 % vs. 95.3 %, p=0.2). Competing-risk regression analysis also failed to demonstrate a difference in cancer-specific mortality [34]. A bi-institutional Mayo Clinic and Memorial Sloan Kettering study compared outcomes between RN (n=286) and PN (n=873) for T1b tumors. Type of surgery was not a significant factor in multivariate modeling of death from RCC (hazard ratio for RN vs. PN: 1.97, p=0.079) [38]. A retrospective study from seven international centers had similar findings. In this study, the RN (n=576) and PN (n=65) groups had similar rates of cancer-specific death (9 % vs. 6.2 %, p=0.6, respectively) and local recurrence (2.3 % vs. 3.6 %, p=0.5, respectively). Type of surgery had no influence on survival in multivariable analysis (p=0.8) [35]. Single-institution retrospective studies have published comparable local recurrence of 1.7–4.0 % and 5-year cancer-specific survival rates of 93.0–99.0 % [36, 39–41].

>T1 Tumors

Although not widely considered standard of care, PN plays a vital role in treating certain patients with >T1 RCC, such as those who would be rendered dialysis dependent after RN. The European Association of Urology recommends NSS for T2 RCC in "selected patients in experienced centers [2]." In general, the available literature relies on pathologically diagnosed T2-3b and may not be unequivocally applicable to patients with clinically evident T2-3b disease prior to PN. The data from several studies reporting the oncologic outcomes of PN for T2-T3b RCC are reported in Table 13.3. A study from

MD Anderson Cancer Center compared the oncologic efficacy of RN ($n=567$) to PN ($n=34$) for locally advanced RCC. The RN group had larger tumors with more advanced pathologic stage. To control for the more advanced features in the RN group, multivariable Cox modeling was performed. In this analysis which included stage, grade, size, histology, and procedure type, PN versus RN was not an independent indicator of disease recurrence or RCC-specific mortality [42]. Breau et al. published a study comparing outcomes between RN ($n=207$) and PN ($n=69$) in populations matched for stage, tumor size, baseline renal function, age, and gender. There was no difference in the risk of cancer-specific survival (HR 0.80, $p=0.5$) or overall survival (HR 1.11, $p=0.6$) between the two groups [43].

The preceding data supports a role for PN in select cases of advanced RCC. Unlike T1 RCC, however, the oncologic efficacy of PN remains uncertain due to the inherent selection biases in the aforementioned studies. In general, PN should be utilized in locally advanced RCC only in cases that are favorable for NSS and/or in patients where RN would result in hemodialysis dependence.

Preserving Renal Function: The Rationale Behind PN

The relative risks and benefits of localized RCC treatment options extend beyond simply perioperative morbidity and cancer-specific outcomes. Understanding the influence of RN versus PN on postoperative CKD is central to this discussion as advanced stages of CKD have been associated with increased mortality and morbidity [44]. Table 13.4 defines the stages of CKD per National Kidney Foundation Disease Outcomes Quality Initiative CKD classification. The renal transplantation literature has been frequently cited as evidence to support the use of RN in patients with normal contralateral renal function as kidney donors have similar risks of hypertension, renal dysfunction, and death compared to matched populations [45–47]. The donor nephrectomy and RCC populations are considerably different, however, as kidney donors tend to be young and lack medical comorbidities. On the contrary to kidney donors, 26 % of patients with a renal mass and a normal contralateral kidney have preoperative Stage III–V CKD [12], while over 50 % of patients with a renal mass in a solitary kidney have preexisting Stage III–V CKD [48, 49]. Pathologic studies of nonneoplastic parenchymal tissue in nephrectomy specimens also show frequent changes associated with underlying comorbidities. In a study of 110 specimens, only 38 % had normal renal parenchyma, of which a majority exhibited pathologically evident vascular disease [50]. A greater decrement in renal function 6 months after surgery was demonstrated in patients with substantial pathologic abnormalities compared to those with normal renal parenchyma [50]. The prevalence of preoperative CKD in RCC patients combined with the frequency of histologically evident renal parenchymal and vascular abnormalities in nonneoplastic tissue at the time of nephrectomy indicates a potential for significant post-nephrectomy renal impairment.

In 2004 Go et al. published their landmark paper demonstrating a graded association between the degree of CKD and the risk of cardiovascular events, hospitalization, and death [44]. This study included 1,120,295 adult patients in the Kaiser Permanente Renal Registry with a follow-up

Table 13.4 National kidney foundation disease outcomes quality initiative CKD classification [112]

Stage	Description	GFR (mL/min/1.73 m^2)
I	Kidney damage with normal or ↑ GFR	≥90
II	Kidney damage with mild ↓ GFR	60–89
III	Moderate ↓ GFR	30–59
IV	Severe ↓ GFR	15–29
V	Kidney failure	< 15 (or dialysis)

interval of 2.84 years. GFR was estimated using the Modification of Diet Renal Disease (MDRD) equation. Multivariable analysis controlling for demographics and comorbidities was performed to elucidate the relationship between CKD stage and adverse patient outcomes. A GFR >60 mL/min/1.73 m^2 was used as the reference. As GFR decreased, the risk of death increased: hazard ratio (HR) = 1.2 for GFR 45–59 mL/min/1.73 m^2, HR = 1.8 for GFR 30–44 mL/min/1.73 m^2, HR = 3.2 for GFR 15–29 mL/min/1.73 m^2, and HR = 5.9 for GFR <15 mL/min/1.73 m^2. The adjusted hazard ratios for cardiovascular events and hospitalization also increased inversely with respect to GFR [44]. A study of 15,837 randomly selected patients from the Third National Health and Nutrition Examination Survey confirms the association between CKD and cardiovascular health. After adjustment in multivariable analysis, the presence of increasing numbers of cardiovascular risk factors was associated with a GFR <60 mL/min/1.73 m^2 (odds ratio for 0, 1, and 2 risk factors = 1, 3.7, 10.4, respectively, $p \leq 0.001$) [51].

In the early 2000s, investigators from both Memorial Sloan Kettering and Mayo Clinic reported a higher rate of renal failure (defined as serum creatinine >2.0 mg/dL) after RN compared to PN [32, 52]. More recently, Huang et al. published a retrospective cohort study from Memorial Sloan Kettering using the MDRD equation to estimate GFR in 662 patients with a single ≤4 cm renal tumor and normal contralateral renal function. RN compared to PN was associated with a lower 3-year postoperative probability of freedom from both GFR <60 mL/min/1.73 m^2 (35 % vs. 80 %, $p < 0.0001$) and GFR <45 mL/min/1.73 m^2 (64 % vs. 95 %, $p < 0.0001$). RN was an independent risk factor for the development of both GFR <60 mL/min/1.73 m^2 (ratio = 3.82, $p < 0.0001$) and GFR <45 mL/min/1.73 m^2 (hazard ratio = 11.8, $p < 0.0001$) [12].

Recently, several investigators have addressed whether enhanced renal preservation via NSS translates into improved overall survival and decreased risk of cardiovascular events compared to RN. Huang et al. performed an analysis of SEER-Medicare consisting of 2,547 RN patients and 556 PN patients with T1a RCC. On multivariable analysis, RN was independently associated with an increased risk of cardiovascular events (hazard ratio = 1.4, $p < 0.05$) and overall mortality (hazard ratio = 1.38, $p < 0.001$). There was no association between RN and cardiovascular death or time to first cardiovascular event [13]. In a study from Mayo Clinic of ≤4 cm renal tumors, RN compared to PN was not associated with worse overall survival when analyzing the entire cohort. In patients <65 years, however, RN was associated with an increased risk of overall mortality (relative risk = 2.16, $p = 0.02$) after adjusting for several factors including comorbidities, preoperative creatinine, and year of surgery [53]. The trend toward improved overall survival with PN compared to RN has been studied in T1b renal tumors as well. Weight et al. reported a retrospective study of 212 PN and 298 RN patients with preoperative GFR > 60 mL/min/1.73 m^2 and a normal contralateral kidney. New onset CKD was defined as postoperative GFR <60 mL/min/1.73 m^2. RN increased the odds of new onset CKD (odds ratio = 3.4, $p < 0.001$) when controlling for gender, age, comorbidities, and preoperative renal function. Cancer-specific survival was equivalent between the two groups when adjusted for stage and grade. Multivariable models indicated that PN (hazard ratio = 0.47, $p = 0.03$) and graded stratification of postoperative renal function ($p = 0.003$) independently predicted overall survival when controlling for pathologic stage, age, and comorbidities [39].

Although the preceding evidence suggests that relative renal preservation by PN is associated with improved overall survival, several questions remain. Foremost, EORTC 30904 failed to show a survival benefit with PN [33]. The limitations of this study are discussed in detail in the previous section. In brief, the small number of overall deaths and lack of reported renal function outcomes clouds the interpretation of the results relating to the effects of renal function on overall survival. Also, future studies will be required to elucidate the relative contributions of "surgically induced" renal failure and the continued effects of medical renal disease in postoperative patients. When planning surgery in RCC patients, urologists must consider the effects of surgical

approach (RN vs. PN) on both oncologic control and renal function given the deleterious effects of CKD on postoperative morbidity and mortality.

Underutilization of PN

Despite equivalent oncologic outcomes and the potential benefits of minimizing postoperative CKD risk, PN remains underutilized. Data from the Nationwide Inpatient Sample compiled from 2003 to 2008 demonstrates that RN consisted of 79.3 % of renal surgeries, while PN comprised the remaining 20.7 % [54]. There was a trend toward increasing PN use over the study interval ($p < 0.001$) [54], and also the overall percentage of PN increased from a previous Nationwide Inpatient Sample study from 1988 to 2002 [55]. The Nationwide Inpatient Sample does not include information on tumor size, location, or histology. Given the downward stage migration of RCC, however, one would assume that a greater portion of detected renal masses would be amenable to NSS than the 20.7 % frequency of PN reported in the most recent Nationwide Inpatient Sample data. Although not the only criteria impacting PN feasibility, tumor size is an important determinant in tumor complexity and is available in the SEER database. Dulabon et al. reported the use of PN in 18,330 patients from the SEER registry with ≤4 cm renal tumors from 1999 to 2006. Six thousand four hundred and sixty (35 %) patients underwent PN and the ratio of PN to RN increased every year ($p < 0.001$) with PN comprising 45 % of renal surgeries in 2006. Additional analysis demonstrated noteworthy disparities in PN utilization with women, elderly, rural, earlier year of surgery, and larger tumor size all having statistically significant adverse effect in predicting PN [56].

Compared to population-based studies, tertiary care centers perform a higher percentage of PNs for T1 renal tumors. In a study of six European centers from 2004 to 2007, PN comprised 86.3 % of renal surgeries for <2 cm tumors, 69.3 % of renal surgeries for 2.1–4 cm tumors, and 35.3 % of renal surgeries for 4.1–7 cm tumors [57]. Investigators from Memorial Sloan Kettering report a similar trend with an increasing usage of PN from 2000 to 2007. In 2007, the frequency of PN was 89 % for tumors ≤4 cm and 60 % for tumors 4.1–7 cm [58]. Future endeavors aimed at understanding the underlying rationale for PN underutilization and addressing these issues are paramount for widespread acceptance of PN throughout the urologic community.

Objective Analysis of Tumor Complexity

In the 2009 AUA small renal mass guideline, it was stated that for clinical T1 renal masses, "nephron sparing approaches should be used whenever feasible"[1]. Partial nephrectomy feasibility was not defined. Differences in opinion between surgeons regarding the feasibility of partial nephrectomy may contribute to the variability in the use of partial nephrectomy described above. An important characteristic that determines whether or not partial nephrectomy is feasible is the technical complexity of the tumor [59]. Traditionally, tumors were described with non-standardized, subjective terms such as central, hilar, deep, superficial, exophytic, or endophytic. This descriptive approach was not quantifiable for research or comparative studies, making it impossible to compare series, techniques, or surgeons with rigor. Inability to quantify tumor complexity may contribute to lack of uniformity in the assessment of partial nephrectomy feasibility and, consequentially, may lead to variability in care of the small renal mass.

Starting in 2009, three systems were introduced that aimed to quantify the anatomical characteristics of renal masses in a reproducible way with meaningful clinical correlation: the RENAL nephrometry score, the Centrality index (C index), and the PADUA classification [60–62]. The RENAL nephrometry scoring system was described by Uzzo in 2009 (Table 13.5) [60]. Points are assigned to four morphometric tumor variables: diameter, exophytic versus endophytic properties, proximity to collecting system or renal sinus, and the tumor's location relative to the polar lines and axial midline (Fig. 13.1).

Table 13.5 RENAL nephromery scoring system

Variable	1 point	2 points	3 points
Diameter (cm)	≤4	>4 and <7	≥7
Exophytic	≥50 %	<50 %	100 % endophytic
Nearness to collecting system or renal sinus (mm)	≥7	>4 and <7	≤4
Anterior/posterior	Qualitative descriptor of "a," "p," or "x"; no points		
Location relative to polar lines	Above upper or below lower polar line	Crosses polar line	More than 50 % across polar line, entirely between polar lines, or crosses axial midline

Kutikov and Uzzo [60]

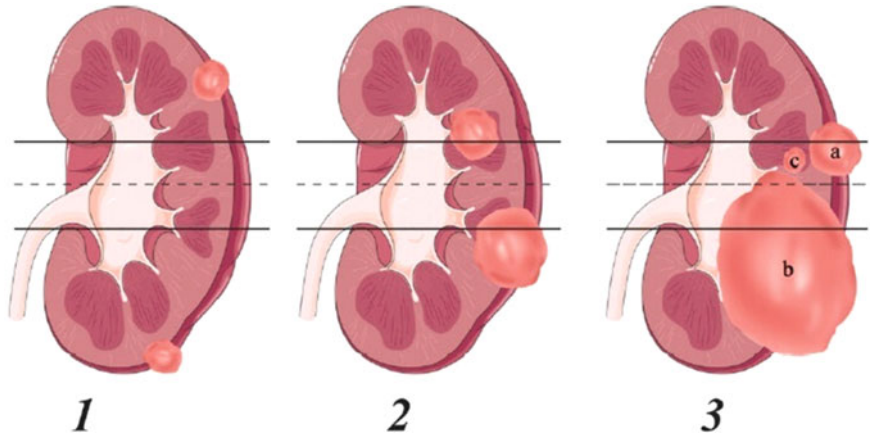

Fig. 13.1 The L component of RENAL nephrometry score characterizes a tumor location relative to the polar lines. A sagittal depiction of the kidney demonstrates the polar lines (*solid*) and renal axial midline (*dashed*), with the points (1, 2, or 3) that would be assigned to each tumor (Permission to reprint is pending from Kutikov A and Uzzo RG [60])

Points are added together with total scores of 4–6, 7–9, and 10–12 corresponding to low, moderate, and high tumor complexity, respectively. A qualitative descriptor "h" is added after the nephrometry score if the lesion abuts the main renal artery or vein. A second descriptive term is added to describe the tumor's anterior (a) or posterior (p) location (or "x" if the tumor cannot be described as anterior or posterior).

The Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) Classification schema shares many similarities with the RENAL nephrometry score [62]. Points are also assigned to anatomical features, and an "a" or "p" classifier is also used to denote anterior or posterior location, respectively (Table 13.6).

The Centrality index (C index) also aims to quantify the complexity of renal masses, but does so with a geometric approach [61]. The Centrality index assesses the proximity of the tumor center to the kidney center and puts this value in context of the tumor size (Fig. 13.2). This schema makes use of the Pythagorean theorem in which the square of the hypotenuse (c) of a right angle triangle is equal to the sum of the squares of the other two sides (a and b) of the triangle (i.e., $a^2+b^2=c^2$). Using axial imaging, the vertical distance from the kidney center to the level of the maximum tumor diameter is measured, as is the horizontal distance from the kidney center to the tumor center. The hypotenuse is then the distance from the kidney center to the tumor center (c).

Table 13.6 The PADUA classification scoring schema [62]

Variable	1 point	2 points	3 points
Polar location	Polar	Interpolar	–
Exophytic	≥50 %	<50 %	100 % endophytic
Renal rim	Lateral	Medial	–
Renal sinus	Uninvolved	Involved	–
Collecting system	Uninvolved	Displaced or invaded	–
Diameter (cm)	≤4	>4 and ≤7	>7

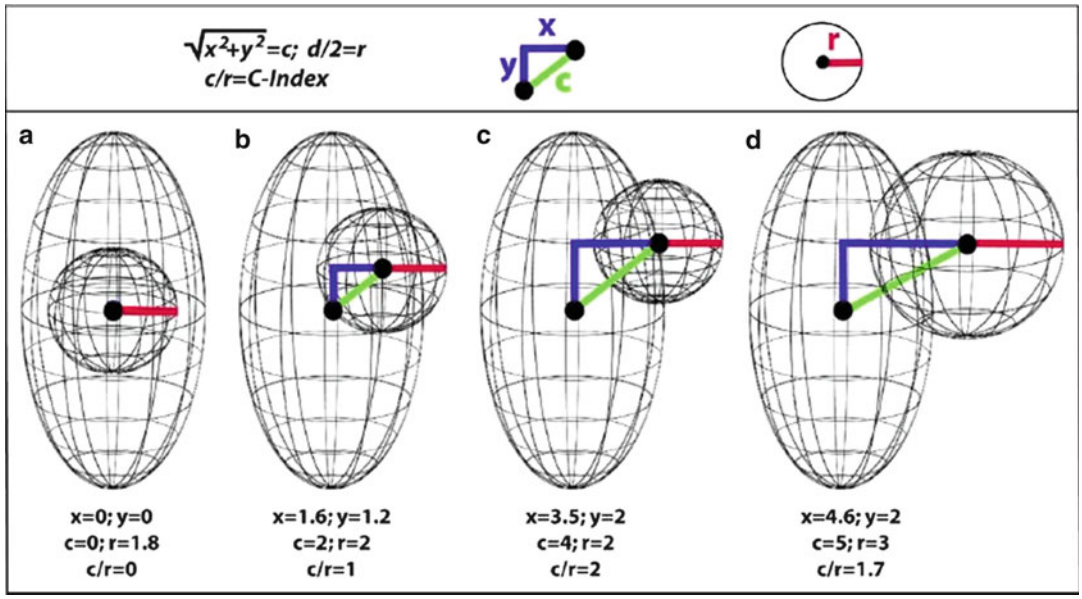

Fig. 13.2 The C index method uses the Pythagorean theorem to measure the distance between kidney center and tumor center, *c* (*green line*), which is the hypotenuse of a triangle formed by *x* and *y* (*blue lines*). Dividing *c* by *r* (*red line*) yields the C index (Permission to reprint is pending from Simmons et al. [61])

The tumor radius (r) is measured. The C index is calculated, where C index = c/r. A C index of 0 indicates that the tumor center is in the kidney center, while a C index of 1 indicates that the tumor periphery abuts the kidney center. The larger the C index, the further is the tumor center from the kidney center.

There is retrospective evidence that these morphometric systems correlate with clinical markers of complexity, in particular a surgeon's choice of operation and approach, surgical technique including ischemia time and parenchymal preservation, as well as surgical outcomes and pathology. In a 2009 survey of the members of the American Urologic Association, respondents were shown 8 tumors with RENAL nephrometry scores ranging from 4 to 10 [59]. On multivariate analysis, each additional RENAL nephrometry score point increased the odds of a surgeon choosing to perform a radical nephrectomy instead of partial nephrectomy (OR 1.59, 95 %, CI 1.27–1.95). Respondents who were more likely to choose partial nephrectomy were high-volume kidney surgeons (OR 1.57), high-volume partial nephrectomy surgeons (OR 3.7), younger (OR 1.64), and in academic practice (1.80). The willingness of a surgeon to perform partial nephrectomy appears to be linked to tumor complexity, but the complexity threshold that triggers radical nephrectomy appears to vary among surgeons.

These findings are supported by retrospective data from clinical practice. In a single-institution

retrospective review, Broughton et al. assessed 154 patients with clinical T1a renal tumors, of whom 120 (77.9 %) had a planned partial nephrectomy [63]. Independent predictors of planned partial nephrectomy included tumor size, with each 1 cm decrease in diameter increasing the OR of partial nephrectomy 2.2-fold ($p=0.011$). Tumor complexity was also an independent predictor, with each 1 point decrease in RENAL nephrometry score increasing the OR of partial nephrectomy 2.4-fold ($p<0.001$). Similar retrospective studies have shown that increasing RENAL nephrometry score is significantly associated with the use of radical as opposed to partial nephrectomy and open as opposed to minimally invasive partial nephrectomy [64, 65].

The morphometric systems have also been found to correlate with technical aspects of partial nephrectomy including ischemia time and percentage of functional kidney volume preserved [66–69]. In a single-institution retrospective review, Simmons et al. calculated RENAL nephrometry score and C index for 237 partial nephrectomy patients and estimated the percentage of functional kidney volume that was preserved using postoperative imaging [69]. They noted that increasing tumor complexity was associated with parenchymal loss, with each 1 unit increase in RENAL nephrometry score correlating with a 5 % decrease in functional volume preservation. Similarly, each 0.5 unit decrease in C index correlated with a 3 % decrease in functional volume preservation.

Higher PADUA and RENAL nephrometry scores and lower C index have been associated with a higher risk of overall complications, including urine leak [62, 66, 67, 70, 71]. In addition, the morphometric systems may also be predictive of renal functional outcomes. For instance, the rate of ≥30 % decrease in estimated GFR was significantly higher among patients with a C index ≤2.5 than those with C index >2.5 (70 % vs. 32 %, $p<0.01$) [67].

It appears that quantitative scoring of tumor complexity by RENAL nephrometry score, PADUA classification, and C index may be a valuable addition to the clinical research armamentarium. The relative predictive abilities of the three systems remain unclear. Comparative research is needed, as are efforts to delineate the role of these systems in determining the feasibility of partial nephrectomy in moderate and highly complex lesions.

Preoperative Evaluation

A thorough preoperative evaluation is essential for patients undergoing open partial nephrectomy. The goals of the preoperative evaluation are clinical TNM staging, identification and treatment of comorbid disease, selecting the proper patients for surgery, as well as reducing the risk of perioperative complications.

Cardiopulmonary Evaluation

Preoperative vigilance may identify patients at elevated risk of cardiopulmonary complications and allow for presurgical intervention. It has been recommended that cardiologists should evaluate and treat patients with unstable angina, decompensated heart failure, arrhythmias, substantial heart valve disease, and known or suspected coronary artery disease prior to noncardiac surgery [72]. A urologist should also inquire about cardiovascular symptoms and risk factors and refer for evaluation accordingly. Risk stratification tools such as the Revised Cardiac Risk Index may be helpful for preoperative risk stratification. The Revised Cardiac Risk Index is composed of six independent predictors of cardiac complications after major noncardiac surgery: high-risk surgical procedure (intraperitoneal, intrathoracic, suprainguinal vascular), ischemic heart disease, congestive heart failure, cerebrovascular disease, preoperative insulin use, and preoperative serum creatinine >2 mg/dL [73].

Predictors for pulmonary complications following noncardiothoracic surgery include chronic obstructive pulmonary disease, age >60 years, smoking, American Society of Anesthesiologists (ASA) class ≥2, inability to perform activities of daily living, congestive heart failure, pulmonary hypertension, and low serum albumin [74, 75].

Patients without these risk factors may still be at risk for pulmonary complications due to surgical positioning and the surgical wound, since upper abdominal surgery and surgery that lasts >3 h are both independent predictors of pulmonary complications [75]. A pulmonary evaluation with chest X-ray, arterial blood gas, pulmonary function tests, and consultation by a pulmonologist may benefit some of these patients. Smokers should quit prior to surgery [74]. An anterior surgical approach may be preferable to a flank approach in patients with pulmonary risk factors.

Renal Evaluation

Assessment of renal function by urinalysis and serum creatinine is mandatory before open partial nephrectomy, especially in light of the high rate of preexisting chronic kidney disease among patients with renal tumors [12]. Methods of estimating kidney function include serum creatinine, 24-h creatinine clearance, radionuclide imaging such as technetium-99 diethylenetriamine pentaacetic acid, or estimating GFR using equations such as the Modification of Diet in Renal Disease (MDRD) equation [76]. Although serum creatinine and estimates of GFR based on serum creatinine such as the MDRD equation may not be as accurate as a 24-h urine collection or radionuclide imaging, they are commonly employed, relatively inexpensive, and typically adequate for clinical purposes.

Imaging

Adequate preoperative imaging is mandatory to identify locally advanced tumors or metastatic disease, as well as to define regional anatomy and to characterize the renal vasculature. Renal angiography used to be commonly employed prior to partial nephrectomy, but it has been replaced by 3D CT angiography at most centers. CT angiography is noninvasive and provides detailed anatomical images by incorporating arteriography, venography, excretory urography, and CT data into a single imaging modality. CT can delineate renovascular anatomy including the subsegmental branches supplying the tumor as well as renal tumor location, depth, and proximity to the collecting system [77]. In addition, preoperative imaging helps identify surgically relevant anatomical variants such as multiple renal arteries, retroaortic or circumaortic left renal vein, and duplex collecting system.

Prophylaxis

Partial nephrectomy patients should have a preoperative urinalysis and culture to screen for bacteriuria. If a urinary tract infection or bacteriuria is discovered, antibiotics should be administered to sterilize the urine prior to surgery, especially in lesions in which collecting system entry is anticipated. The American Urologic Association recommends mechanical prophylaxis (intermittent pneumatic compression devices or compression stockings) in all patients undergoing open surgery and consideration of pharmacologic prophylaxis in patients with elevated risk for VTE [78, 79]. The use of pharmacologic VTE prophylaxis in partial nephrectomy is controversial [80].

Surgical Techniques

Broadly speaking, the steps of performing open partial nephrectomy are the incision and surgical approach, isolation and control of the renal hilum, mobilization of the kidney while preserving the perinephric fat overlying the tumor, and tumor excision. This is followed by renorrhaphy with hemostasis, collecting system repair if needed, and repair of the parenchymal defect.

Approach

Choosing a favorable surgical approach is the first step in a successful partial nephrectomy. The ideal approach provides excellent access to the kidney, renal vasculature, and tumor while minimizing wound-related morbidity. The position of the kidney relative to the ribs impacts the level of a flank

incision and should be assessed on preoperative radiographic studies. Other factors to consider include the tumor location and size.

There are numerous surgical approaches to the kidney. For partial nephrectomy, the primary approaches are the supracostal flank, transcostal (classic) flank, and anterior subcostal incisions. Turner-Warwick described a rib-sparing extraperitoneal, extrapleural supracostal flank incision that is favored at some institutions [81]. For very large upper pole tumors, a thoracoabdominal approach can be useful. An 8-cm "mini-flank" supra 11th rib incision has been described as an effective alternative for radical or partial nephrectomy [82]. Other approaches to the kidney such as anterior midline, the dorsal lumbotomy, and subcostal flank incision are rarely if ever the most favorable approach for partial nephrectomy.

Vascular Control

After the surgical approach is complete and retraction is in place, controlling the renal pedicle is the initial priority with rare exceptions. The main renal artery and vein should be carefully dissected from surrounding structures. Vessel loops can be used to encircle the renal artery and vein without compromising blood flow. Establishing control of the renal vasculature gives the surgeon the ability to rapidly occlude the artery if necessary to stop unanticipated and uncontrolled bleeding.

Kidney Mobilization

Having established vascular control, one can proceed with mobilizing the remainder of the kidney. Gerota's fascia is opened. The ureter should be indentified to reduce risk of ureteral injury. It can be tagged with a vessel loop for identification. Great care should be taken to avoid injuring its blood supply. The kidney is mobilized within the perirenal fat, though the fat overlying the tumor should be left undisturbed in case there has been occult fat invasion. Mobilizing the kidney within the fat can be performed sharply or with cautery. It can be time consuming and challenging in patients with prior kidney infections or other inflammatory processes that result in "sticky fat." Nevertheless, adequate mobilization of the kidney is an essential step in a high-quality, safe partial nephrectomy.

Vascular Clamping

During tumor excision and portions of renorrhaphy, the segmental artery supplying the tumor or the main renal artery is temporarily occluded with a vascular clamp. The purpose of clamping is to reduce intraoperative bleeding and improve visualization. Another proposed benefit is to ease access to intrarenal structures by reducing tissue turgor.

Mannitol is given intravenously 5–10 min before temporary renal arterial occlusion [83–85]. Anticoagulation to prevent intrarenal thrombosis is not necessary. The renal vein is not clamped, which may permit some oxygenation despite arterial occlusion [86–88]. In open partial nephrectomy, the kidney is cooled immediately after clamping to protect against ischemic renal injury. The entire kidney is surrounded by ice slush for 10–15 min to obtain a core kidney temperature of approximately 20° C, which permits as much as 3 h of ischemia time [85]. In cases where ischemia time is anticipated to be short, warm ischemia may be a reasonable option. Safe limits of warm ischemia have been proposed. Limits of 20 and 35 min have recently been advocated as safe [84, 89]. Nonetheless, some data suggests that there is no safe limit of warm ischemia, with each additional minute increasing the risk of acute renal failure, chronic kidney disease, and end-stage renal disease [90].

Excision of the Tumor

Once clamped and cooled, partial nephrectomy can proceed. There are various techniques of partial nephrectomy that can be employed, but all aim to fully excise the tumor with reliably negative margins and maximal preservation of

functional parenchyma. There are a variety of partial nephrectomy techniques which include simple enucleation, polar nephrectomy, heminephrectomy and wedge resection, or resection of the tumor with a thin rim of normal parenchyma.

In enucleation, the tumor is separated from the surrounding normal parenchyma along a natural plane provided by the tumor pseudocapsule. No margin of normal parenchyma is taken. Most often, this technique is employed in patients with an inherited kidney cancer syndrome or multiple tumors [91]. Enucleation has traditionally been avoided in sporadic RCC due to concerns about local recurrence, as the tumor may extend for several millimeters through the pseudocapsule [92–95]. When enucleation is employed, it may be beneficial to ablate the resection margin to reduce the risk of recurrence [96]. In most cases, techniques that remove the tumor along with a margin of normal parenchyma are preferable to enucleation.

Polar nephrectomy can be employed for tumors that are limited to one pole of the kidney. Traditionally, this technique involved ligating and dividing the segmental apical or basilar artery supplying the upper or lower pole of the kidney, respectively. This selective vascular control results in a line on the kidney surface demarcating the ischemic pole from the rest of the kidney that remains perfused. The ischemic, tumor-bearing pole of the kidney is then excised along the line of ischemia. An alternative approach that we favor is to define the limits of resection by a thin rim of normal parenchyma around the tumor and not by the territory supplied by the segmental artery. This permits preservation of polar parenchyma that is uninvolved by tumor. Large tumors that extensively involve the upper or lower portion of the kidney should be excised by heminephrectomy.

Centrally located tumors can prove particularly challenging given their intimate association with the renal hilum and collecting system. One option is to create an overlying radial or Y-shaped nephrotomy to expose the underlying tumor, which can then be excised by enucleation or with a thin rim of parenchyma. Alternatively, the tumor can be approached via the hilum using the intrarenal surgical techniques of Gil Vernet. Small intrarenal venous branches can be ligated to improve exposure without compromising venous return. Segmental arteries supplying the tumor are divided. The tumor is excised, along with neighboring renal sinus fat if possible. Often, no normal adjacent tissue can be excised and the tumor is essentially enucleated from the sinus.

Regardless of the surgical technique employed in partial nephrectomy, complete tumor excision should be confirmed in the operating room. Intraoperative ultrasound can be employed to prospectively delineate resection margins and to identify additional occult tumors that are a source of ipsilateral recurrence [97, 98]. Frozen section can be employed to evaluate for margin status. As long as the margin is negative, the size of the negative margin is not thought to be important [99].

Renorrhaphy

After excision of the tumor, the transected blood vessels on the renal surface are secured with figure-of-eight 4-0 Monocryl sutures. The argon beam can used to achieve hemostasis on the renal cortex, but it should be used with caution as it may disrupt sutures or injure the collecting system. Openings in the collecting system should be carefully repaired with 4-0 Monocryl sutures. One can improve identification of collecting system defects by injecting methylene blue or indigo carmine either intravascularly or directly into the renal pelvis. Although it is rarely necessary, a ureteral stent can be placed in a retrograde fashion at the start of the procedure if significant repair of the intrarenal collecting system is anticipated. Alternatively, a stent can be placed antegrade over a wire through the opening in the collecting system.

Once suturing of vessels and collecting system is complete, a bolster can be placed in the defect, though this is often not necessary if the cortical edges can be adequately opposed. The bolster can be composed of rolled Surgicel® or other absorbable hemostatic products. Floseal® (Baxter International Inc, Deerfield, IL, USA) or other hemostatic gels can also be used. The edges of the renal cortex are reapproximated, over the

bolster if one is used, with pledgeted interrupted 2-0 polyglactic sutures, ensuring that the renal vessels are not kinked or obstructed. These can be secured with knots or with a Weck clip (Pilling Weck Canada, L.P., Markham, ON, Canada) and a Lapra-Ty® clip (Ethicon Endo-Surgery, Cincinnati, OH, USA). If the renal artery was clamped, it can be unclamped immediately after obtaining hemostasis or after the entire renorrhaphy is complete. A retroperitoneal drain should be placed, but can be omitted in small, superficial tumors in which the collecting system was not entered [100].

Addressing the Adverse Impact of Ischemia

Partial nephrectomy can be associated with a postoperative decline in renal function [86, 101, 102]. Numerous factors contribute to the decline in GFR after partial nephrectomy, including those that are not modifiable such as older age, female gender, larger tumor size, as well as solitary kidney and preexisting renal dysfunction [86, 101, 102]. Modifiable factors that contribute to decreased GFR include reduction in functional renal parenchyma and ischemic injury [83, 90, 102–104]. Even when accounting for the percent of functional renal parenchyma preserved after partial nephrectomy, renal ischemia is independently associated with postoperative renal dysfunction [104]. In a bi-institutional study of nephron-sparing surgery in solitary kidneys, warm and cold ischemia were associated with higher risk of acute ($p<0.001$) and chronic ($p=0.027$) renal failure, need for temporary dialysis ($p=0.028$), as well as urine leak ($p=0.006$) when compared to partial nephrectomy without clamping [89].

To address the adverse impact of renal ischemia, several investigators have proposed performing partial nephrectomy with the kidney fully perfused [48, 105–108]. We, thus far, at the Lahey Clinic have performed 839 open non-clamping partial nephrectomies and have demonstrated that this can be safely performed for complex lesions. In addition we have compared this patient population to 380 patients who had renal artery clamping, and the observations with regard to blood loss, pre- and post-op creatinine levels, urine leaks, and oncologic outcomes are recorded (Table 13.7). In an open non-clamping series in 158 patients with solitary kidney, 16 % of patients had previous ipsilateral nephron-sparing surgery, 33 % of tumors were characterized as hilar/central, and mean tumor size was 3.6 cm. The maximum tumor size in the series was 13 cm, and while the median number of tumors resected was 1, the series included patient who underwent multiple partial nephrectomy of as many as 13 tumors [48].

Table 13.7 Clamp versus non-clamp

	Clamp	Non-clamp
	380 Pts	839 Pts
Blood loss (med)	250	600
Creatinine (avg)	pre-op 1.16	pre-op 1.15
	latest 1.8	latest 1.4
Urine leak (pts)	8 (2 %)	31 (4 %)
Regional/local Recurrence	12 (3 %)	24 (3 %)
Other metastasis	23 (6 %)	36 (4 %)

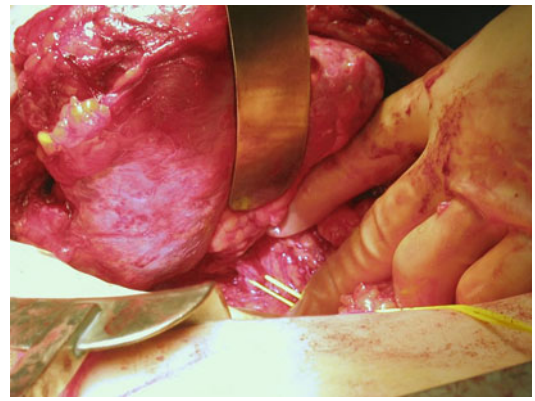

Fig. 13.3 Vascular control

The open non-clamping technique has been described in detail [48, 105]. The kidney is mobilized as described above. Similar to clamping partial nephrectomy, the hilar vessels are dissected out and non-occlusive control is obtained with vessel loops in case vessel clamping is needed (Fig. 13.3). The perirenal fat overlying the tumor is left in situ (Fig. 13.4). Margins are marked out with the aid of intraoperative ultrasound.

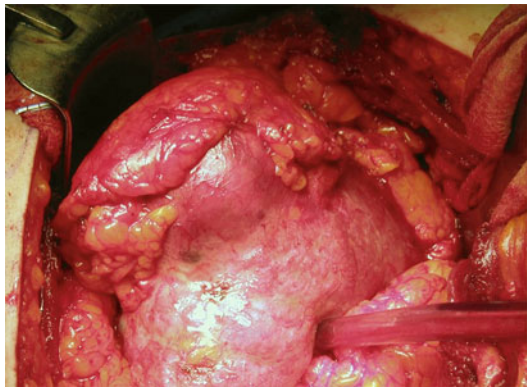

Fig. 13.4 Preservation of perinephric fat

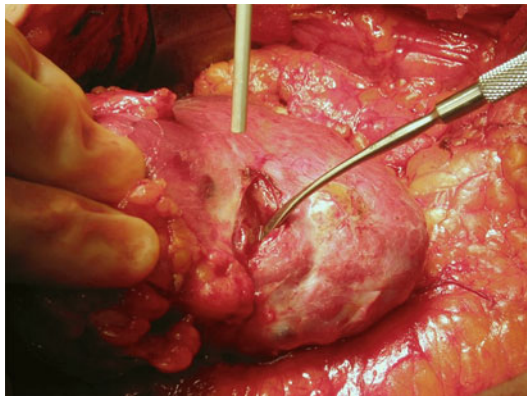

Fig. 13.5 Cleavage plane between tumor and normal parenchyma

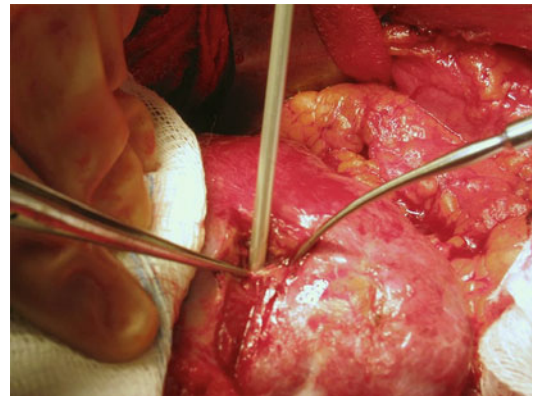

Fig. 13.6 Coagulation of small arteries at the corticomedullary junction

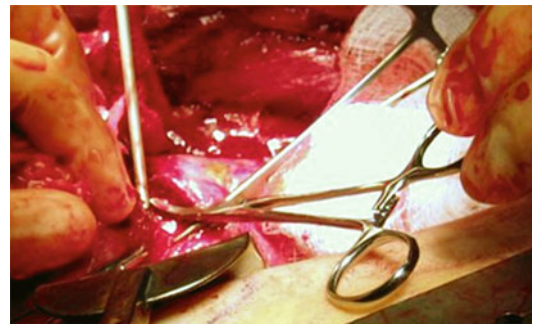

Fig. 13.7 Ligation of larger intrarenal arteries at tumor base

The renal capsule is opened either sharply with tenotomy scissor or with handheld electrocautery. The renal parenchyma is opened with a tenotomy scissor circumferentially. Penfield dissectors are used to split the parenchyma, leaving a thin rim of grossly normal parenchyma on the tumor (Fig. 13.5). A Frazier pediatric suction is used to keep the base of the nephrotomy free of blood. It also serves to locate cortical vessels which can be either coagulated if small or tied with 4–0 absorbable suture and divided (Fig. 13.6). At the base of the tumor, the specimen is gently lifted and the remaining larger vessels can be clamped with a small right angle clamp, divided and tied (Figs. 13.7, 13.8; Video 13.1). The specimen is inked to grossly evaluate resection margins. Frozen sections can be obtained if there is any question of a positive margin. In the case of a positive margin, additional tissue can be resected. Hemostasis and renorrhaphy proceed as described above. On advantage of non-clamping is that indigo carmine can be given intravenously to permit evaluation for openings in collecting system. In cases of brisk hemorrhage, which is rare with experience, the surgeon can either clamp the renal vessels, apply manual compression adjacent to the cut renal parenchyma, or apply pressure with a Kittner dissector to a bleeding vessel. The non-clamping technique allows excellent preservation of normal parenchyma, even with entirely endophytic tumors which can be approached through the hilum and sinus using Gil Vernet's techniques and selective ligation of tertiary and quaternary arteries or via a capsular nephrotomy.

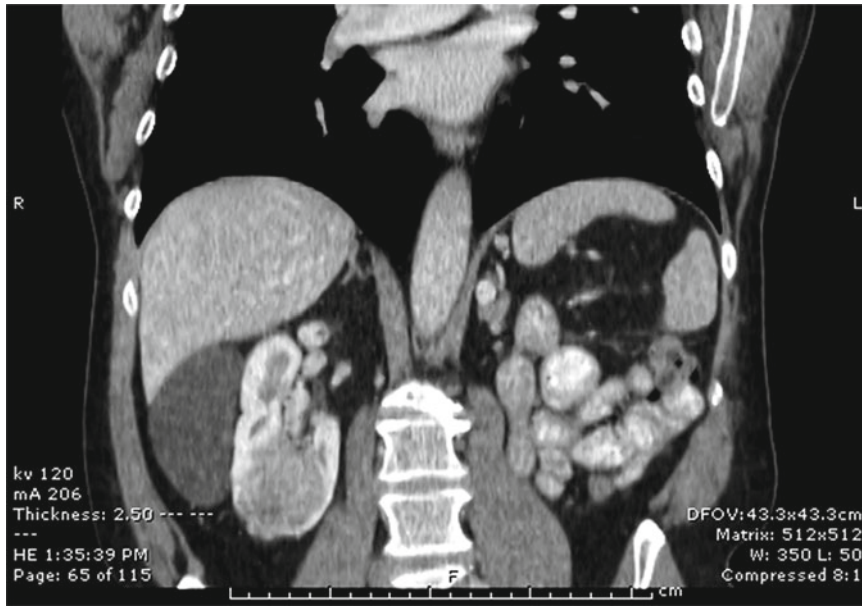

Fig. 13.8 Lower pole tumor – solitary kidney

In non-clamping partial nephrectomy series, in 158 solitary kidneys, there was a trend toward lower percentage decrease in nadir GFR when measured between 7 and 100 days postoperatively in the non-clamping cohort versus the clamping cohort (11.0 % vs. 16.1 %, $P=0.08$) [48]. The data suggest a progressive renal insult after 100 days in the clamping group. **When measured 101 and 365 days after surgery in comparison to preoperative values, there was a 27.7 % decrease in GFR in the clamping group compared to 11.8 % in the non-clamping group** (***P*=0.01**). A multivariate analysis that included tumor size, location, and focality as well as CKD risk factors was performed. Clamping was the only significant covariate. A limitation is that this multivariate analysis did not account for percent of functional parenchyma preserved, though another series suggests that ischemic injury remains an important determinant of postoperative renal failure even when accounting for percent of parenchyma that is preserved [104]. There was no difference in median estimated blood loss between the non-clamping and clamping groups (900 vs. 1,000 mL, P=0.86). The 5-year RCC-specific survival (excluding patients undergoing cytoreductive nephrectomy) was also similar between the non-clamping and clamping cohorts (79 % vs. 75 %, $P=0.68$). Of note, while it is theorized that clamping may improve visualization, this does not translate into better margins. In patients with two functioning renal units, margin rates were similar between the clamping and non-clamping groups (6 % vs. 4.7 %)[105].

References

1. Campbell SC, Novick AC, (null), Blute ML, Chow GK, Derweesh IH, et al. Guideline for Management of the Clinical T1 Renal Mass. Elsevier Inc; 2009;182(4):9.
2. Ljungberg B, Cowan NC, Hanbury DC, Hora M, Kuczyk MA, Merseburger AS, et al. EAU guidelines on renal cell carcinoma: the 2010 update. Eur Urol. 2010;58(3):398–406.
3. Herr H. A history of partial nephrectomy for renal tumors. J Urol Elsevier. 2005;173(3):705–8.
4. Herr HW. Surgical management of renal tumors: a historical perspective. Urologic clinics of North America. Elsevier. 2008;35(4):543–9.
5. Bell E. A classification of renal tumors with observations on the frequency of the various types. J Urol. 1938;39:238.
6. Vermooten V. Indications for conservative surgery in certain renal tumors: a study based on the growth pattern of the cell carcinoma. J Urol. 1950;64(2):200–8.

7. Zinman L, Dowd JB. Partial nephrectomy in renal cell carcinoma. Surg Clin North Am. 1967;47(3): 685–93.
8. WICKHAM JEA. Conservative renal surgery for adenocarcinoma. The place of bench surgery. Br J Urol. 1975;47(1):25–36.
9. Licht MR, Novick AC. Nephron sparing surgery for renal cell carcinoma. J Urol. 1993;149(1):1–7.
10. Herr HW. Partial nephrectomy for unilateral renal carcinoma and a normal contralateral kidney: 10-year followup. J Urol. 1999;16(1):33–5.
11. Fergany AFA, Hafez KSK, Novick ACA. Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. J Urol. 2000; 163(2):442–5.
12. 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. Lancet Oncol. 2006;7(9): 735–40.
13. 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. discussion61–2.
14. Ferlay J, Shin H-R, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127(12):2893–917.
15. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. 2012;62(1):10–29.
16. Chow W-H, Dong LM, Devesa SS. Epidemiology and risk factors for kidney cancer. Nature Publishing Group; 2010May1;7(5):13.
17. Storkel S, Eble JN, Adlakha K, Amin M, Blute ML, Bostwick DG, et al. Classification of renal cell carcinoma: workgroup No. 1. Union internationale contre le cancer (UICC) and the American joint committee on cancer (AJCC). Cancer. 1997;80(5):987–9.
18. Chow W-H, Devesa SS. Contemporary epidemiology of renal cell cancer. The Cancer J. 2008;14(5): 288–301.
19. Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al. Cancer Incidence in Five Continents. Lyon: International Agency for Research on Cancer; 2007.
20. Hunt JD, van der Hel OL, McMillan GP, Boffetta P. Renal cell carcinoma in relation to cigarette smoking: meta-analysis of 24 studies. Int J Cancer. 2005;114(1):101–8.
21. Chow WH, Gridley G, Fraumeni JF, Järvholm B. Obesity, hypertension, and the risk of kidney cancer in men. N Engl J Med. 2000;343(18):1305–11.
22. Pischon T, Lahmann PH, Boeing H, Tjønneland A, Halkjaer J, Overvad K, et al. Body size and risk of renal cell carcinoma in the European prospective investigation into cancer and nutrition (EPIC). Int J Cancer. 2006;118(3):728–38.
23. Oh SW, Yoon YS, Shin S-A. Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea national health insurance corporation study. J Clin Oncol. 2005;23(21):4742–54.
24. Levi F, Ferlay J, Galeone C, Lucchini F, Negri E, Boyle P, et al. The changing pattern of kidney cancer incidence and mortality in Europe. BJU Int. 2008;101(8):949–58.
25. 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.
26. Cooperberg MR, Mallin K, Ritchey J, Villalta JD, Carroll PR, Kane CJ. Decreasing size at diagnosis of stage 1 renal cell carcinoma: analysis from the national cancer data base, 1993 to 2004. J Urol. 2008;179(6):2131–5.
27. FRANK I, Blute ML, CHEVILLE JC, Lohse CM, WEAVER AL ZINCKEH. Solid renal tumors: an analysis of pathological features related to tumor size. J Urol. 2003;170(6 Pt 1):2217–20.
28. Remzi M, Ozsoy M, Klingler H-C, Susani M, Waldert M, Seitz C, et al. Are small renal tumors harmless? analysis of histopathological features according to tumors 4 cm or less in diameter. J Urol. 2006;176(3):896–9.
29. Pahernik S, Ziegler S, Roos F, Melchior SW, Thüroff JW. Small renal tumors: correlation of clinical and pathological features with tumor size. J Urol. 2007;178(2):414–7. discussion416–7.
30. Nguyen MM, Gill IS. Effect of renal cancer size on the prevalence of metastasis at diagnosis and mortality. The J of Urol. Am Urol Assoc. 2009;181(3):8.
31. Thompson RH, Hill JR, Babayev Y, Cronin A, Kaag M, Kundu S, et al. Metastatic renal cell carcinoma risk according to tumor size. J Urol. 2009;182(1): 41–5.
32. Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. Mayo Clin Proc. 2000;75(12):1236–42.
33. van Poppel H, Da Pozzo L, Albrecht W, Matveev V, Bono A, Borkowski A, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol. 2011;59(4):543–52.
34. Crépel M, Jeldres C, Sun M, Lughezzani G, Isbarn H, Alasker A, et al. A population-based comparison of cancer-control rates between radical and partial nephrectomy for T1A renal cell carcinoma. Urology. 2010;76(4):883–8.
35. Patard J-J, Shvarts O, Lam JS, Pantuck AJ, Kim HL, Ficarra V, et al. Safety and efficacy of partial nephrectomy for all T1 tumors based on an international multicenter experience. J Urol. 2004;171(6 Pt 1):2181–5.
36. Antonelli A, Cozzoli A, Nicolai M, Zani D, Zanotelli T, Perucchini L, et al. Nephron-sparing surgery versus radical nephrectomy in the treatment of intracapsular renal cell carcinoma up to 7 cm. Eur Urol. 2008;53(4):7.

37. Lee CT, Katz J, Shi W, Thaler HT, Reuter VE, Russo P. Surgical management of renal tumors 4 cm. or less in a contemporary cohort. J Urol. 2000;163(3): 730–6.
38. Thompson RH, Siddiqui S, Lohse CM, Leibovich BC, Russo P, Blute ML. Partial versus radical nephrectomy for 4 to 7 cm renal cortical tumors. J Urol. 2009;182(6):2601–6.
39. Weight CJ, Larson BT, Gao T, Campbell SC, Lane BR, Kaouk JH, et al. Elective partial nephrectomy in patients with clinical T1b renal tumors is associated with improved overall survival. Urology. 2010;76(3):631–7.
40. Joniau S, Vander Eeckt K, Srirangam SJ, Van Poppel H. Outcome of nephron-sparing surgery for T1b renal cell carcinoma. BJU Int. 2009;103(10): 1344–8.
41. Pahernik S, Roos F, Röhrig B, Wiesner C, Thüroff JW. Elective nephron sparing surgery for renal cell carcinoma larger than 4 cm. J Urol. 2008;179(1):71–4. discussion74.
42. Margulis V, Tamboli P, Jacobsohn KM, Swanson DA, Wood CG. Oncological efficacy and safety of nephron-sparing surgery for selected patients with locally advanced renal cell carcinoma. BJU Int. 2007;100(6):1235–9.
43. Breau RH, Crispen PL, Jimenez RE, Lohse CM, Blute ML, Leibovich BC. Outcome of stage T2 or greater renal cell cancer treated with partial nephrectomy. J Urol. 2010;183(3):903–8.
44. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C-Y. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004;351(13):1296–305.
45. Ramcharan T, Matas AJ. Long-term (20–37 years) follow-up of living kidney donors. Am J Transplant. 2002;2(10):959–64.
46. Okamoto MM, Akioka KK, Nobori SS, Ushigome HH, Kozaki KK, Kaihara SS, et al. Short- and long-term donor outcomes after kidney donation: analysis of 601 cases over a 35-year period at Japanese single center. Transplantation. 2009;87(3):419–23. CORD Conference Proceedings.
47. Najarian JSJ, Chavers BMB, McHugh LEL, Matas AJA. 20 years or more of follow-up of living kidney donors. Lancet. 1992;340(8823):807–10.
48. Wszolek MF, Kenney PA, Lee Y, Libertino JA. Comparison of hilar clamping and non-hilar clamping partial nephrectomy for tumours involving a solitary kidney. BJU Int. 2011;107(12):1886–92.
49. La Rochelle J, Shuch B, Riggs S, Liang L-J, Saadat A, Kabbinavar F, et al. Functional and oncological outcomes of partial nephrectomy of solitary kidneys. J Urol. 2009;181(5):7.
50. Bijol V, Mendez GP, Hurwitz S, Rennke HG, Nosé V. Evaluation of the nonneoplastic pathology in tumor nephrectomy specimens: predicting the risk of progressive renal failure. Am J Surg Pathol. 2006;30(5):575–84.
51. Foley RN, Wang C, Collins AJ. Cardiovascular risk factor profiles and kidney function stage in the US general population: the NHANES III study. Mayo Clin Proc. 2005;80(10):9.
52. McKiernan J, Simmons R, Katz J, Russo P. Natural history of chronic renal insufficiency after partial and radical nephrectomy. Urology. 2002;59(6): 816–20.
53. 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. discussion472–3.
54. Kim SP, Shah ND, Weight CJ, Thompson RH, Moriarty JP, Shippee ND, et al. Contemporary trends in nephrectomy for renal cell carcinoma in the United States: results from a population based cohort. J Urol. 2011;186(5):1779–85.
55. Hollenbeck BK, Taub DA, Miller DC, Dunn RL, Wei JT. National utilization trends of partial nephrectomy for renal cell carcinoma: a case of underutilization. Urology. 2006;67(2):254–9.
56. Dulabon LM, Lowrance WT, Russo P, Huang WC. Trends in renal tumor surgery delivery within the United States. Cancer. 2010;116(10):2316–21.
57. Zini L, Patard JJ, Capitanio U, Mejean A, Villers A, De La Taille A, et al. The use of partial nephrectomy in European tertiary care centers. Eur J Surg Oncol. 2009;35(6):7. Elsevier Ltd.
58. Thompson RH, Kaag M, Vickers A, Kundu S, Bernstein M, Lowrance W, et al. Contemporary use of partial nephrectomy at a tertiary care center in the United States. J Urol. 2009;181(3):993–7.
59. Weight CJ, Crispen PL, Breau RH, Kim SP, Lohse CM, Boorjian SA, et al. Practice-setting and surgeon characteristics heavily influence the decision to perform partial nephrectomy among American urologic association surgeons. BJU Int. 2012. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1464-410X.2012.11112.x/abstract.
60. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol. 2009;182(3):844–53.
61. Simmons MN, Ching CB, Samplaski MK, Park CH, Gill IS. Kidney tumor location measurement using the C index method. J Urol. 2010;183(5):1708–13.
62. Ficarra V, Novara G, Secco S, Macchi V, Porzionato A, De Caro R, et al. Preoperative aspects and dimensions used for an anatomical (PADUA) classification of renal tumours in patients who are candidates for nephron-sparing surgery. Eur Urol. 2009;56(5): 786–93.
63. Broughton GJ, Clark PE, Barocas DA, Cookson MS, Smith JA, Herrell SD, et al. Tumour size, tumour complexity, and surgical approach are associated with nephrectomy type in small renal cortical tumours treated electively. BJU Int. 2012;109(11):1607–13. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1464-410X.2011.10607.x/abstract.
64. Canter D, Kutikov A, Manley B, Egleston B, Simhan J, Smaldone M, et al. Utility of the R.E.N.A.L. nephrometry scoring system in objectifying treatment

decision-making of the enhancing renal mass. Urology. 2011;78(5):1089–94. Available from: http://www.sciencedirect.com.ezproxyhost.library.tmc.edu/science/article/pii/S0090429511004353.
65. Rosevear HM, Gellhaus PT, Lightfoot AJ, Kresowik TP, Joudi FN, Tracy CR. Utility of the RENAL nephrometry scoring system in the real world: predicting surgeon operative preference and complication risk. BJU Int. 2012;109(5):700–5. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1464-410X.2011.10452.x/abstract.
66. Waldert M, Waalkes S, Klatte T, Kuczyk MA, Weibl P, Schüller G, et al. External validation of the preoperative anatomical classification for prediction of complications related to nephron-sparing surgery. World J Urol. 2010;28(4):531–5. Available from: http://www.springerlink.com.ezproxyhost.library.tmc.edu/content/7l2660p1144761q8/fulltext.pdf.
67. Samplaski MK, Hernandez A, Gill IS, Simmons MN. C-index is associated with functional outcomes after laparoscopic partial nephrectomy. J Urol. 2010;184(6):2259–63.
68. Altunrende F, Laydner H, Hernandez AV, Autorino R, Khanna R, White MA, et al. Correlation of the RENAL nephrometry score with warm ischemia time after robotic partial nephrectomy. World J Urol [Internet]. 2012Apr.19. Available from: http://www.springerlink.com.ezproxyhost.library.tmc.edu/content/7621231072217650/?MUD=MP
69. Simmons MN, Hillyer SP, Lee BH, Fergany AF, Kaouk J, Campbell SC. Nephrometry score is associated with volume loss and functional recovery after partial nephrectomy. J Urol. 2012;188:39.
70. Simhan J, Smaldone MC, Tsai KJ, Canter DJ, Li T, Kutikov A, et al. Objective measures of renal mass anatomic complexity predict rates of major complications following partial nephrectomy. Eur Urol. 2011;60(4):724–30.
71. Bruner B, Breau RH, Lohse CM, Leibovich BC, Blute ML. Renal nephrometry score is associated with urine leak after partial nephrectomy. BJU Int. 2011;108(1):67–72.
72. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. Circulation. 2007. p. e418–99.
73. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100(10):1043–9.
74. Bapoje SR, Whitaker JF, Schulz T, Chu ES, Albert RK. Preoperative evaluation of the patient with pulmonary disease. Chest. 2007;132(5):1637–45.
75. Qaseem A, Snow V, Fitterman N, Hornbake ER, Lawrence VA, Smetana GW, et al. Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American College of Physicians. Ann Intern Med. 2006;144:575–80.
76. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of diet in renal disease study group. Ann Intern Med. 1999;130(6):461–70.
77. Coll DM, Uzzo RG, Herts BR, Davros WJ, Wirth SL, Novick AC. 3-dimensional volume rendered computerized tomography for preoperative evaluation and intraoperative treatment of patients undergoing nephron sparing surgery. J Urol. 1999;161(4):1097–102.
78. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American college of chest physicians evidence-based clinical practice guidelines (8th edition). Chest. 2008;133:381S–453.
79. Forrest JB, Clemens JQ, Finamore P, Leveillee R, Lippert M, Pisters L, et al. AUA best practice statement for the prevention of deep vein thrombosis in patients undergoing urologic surgery. J Urol. 2009;181:1170–7.
80. Kenney PA, Wotkowicz C, Libertino JA. Contemporary open surgery of the kidney. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh urology 10th edition. 10th ed. Philadelphia: Saunders; 2011. p. 1554–627.
81. Turner Warwick RT. The supracostal approach to the renal area. Br J Urol. 1965;37(6):671–2.
82. DiBlasio CJ, Snyder ME, Russo P. Mini-flank supra-11th rib incision for open partial or radical nephrectomy. BJU Int. 2006;97(1):149–56.
83. Simmons MN, Schreiber MJ, Gill IS. Surgical renal ischemia: a contemporary overview. J Urol. 2008;180(1):19–30.
84. Becker F, Van Poppel H, Hakenberg OW, Stief C, Gill I, Guazzoni G, et al. Assessing the impact of ischaemia time during partial nephrectomy. Eur Urol. 2009;56(4):625–34.
85. Novick AC. Renal hypothermia: in vivo and ex vivo. Urol Clin North Am. 1983;10(4):637–44.
86. Clark MA, Shikanov S, Raman JD, Smith B, Kaag M, Russo P, et al. Chronic kidney disease before and after partial nephrectomy. J Urol. 2011;185(1):43–8.
87. Gong EM, Zorn KC, Orvieto MA, Lucioni A, Msezane LP, Shalhav AL. Artery-only occlusion may provide superior renal preservation during laparoscopic partial nephrectomy. Urology. 2008;72(4):843–6.

88. Tracy CR, Terrell JD, Francis RP, Wehner EF, Smith J, Litorja M, et al. Characterization of renal ischemia using DLP hyperspectral imaging: a pilot study comparing artery-only occlusion versus artery and vein occlusion. J Endourol. 2010;24(3): 321–5.
89. Thompson RH FRANKI, Lohse CM, Saad IR, Fergany A, ZINCKE H, et al. The impact of ischemia time during open nephron sparing surgery on solitary kidneys: a multi-institutional study. J Urol. 2007;177(2):471–6.
90. Thompson RH, Lane BR, Lohse CM, Leibovich BC, Fergany A, FRANK I, et al. Every minute counts when the renal hilum is clamped during partial nephrectomy. Eur Urol. 2010;58(3):340–5.
91. Walther MM, Thompson N, Linehan W. Enucleation procedures in patients with multiple hereditary renal tumors. World J Urol. 1995;13(4):248–50.
92. Li QL, Guan HW, Zhang QP, Zhang LZ, Wang FP. Optimal margin in nephron-sparing surgery for renal cell carcinoma 4 cm or less. Eur Urol. 2003;44: 448–51.
93. Blackley SK, Ladaga L, Woolfitt RA, Schellhammer PF. Ex situ study of the effectiveness of enucleation in patients with renal cell carcinoma. J Urol. 1988;140(1):6–10.
94. Marshall FF, Taxy JB, Fishman EK, Chang R. The feasibility of surgical enucleation for renal cell carcinoma. J Urol. 1986;135(2):231–4.
95. Rosenthal CL, Kraft R, Zingg EJ. Organ-preserving surgery in renal cell carcinoma: tumor enucleation versus partial kidney resection. Eur Urol. 1984;10(4):222–8.
96. Kutikov A, Vanarsdalen KN, Gershman B, Fossett LK, Guzzo TJ, Wein AJ, et al. Enucleation of renal cell carcinoma with ablation of the tumour base. BJU Int. 2008;102(6):688–91.
97. Assimos DG, Boyce H, Woodruff RD, Harrison LH, McCullough DL, Kroovand RL. Intraoperative renal ultrasonography: a useful adjunct to partial nephrectomy. J Urol. 1991;146(5):1218–20.
98. Campbell SC, Fichtner J, Novick AC, Steinbach F, Stöckle M, Klein EA, et al. Intraoperative evaluation of renal cell carcinoma: a prospective study of the role of ultrasonography and histopathological frozen sections. J Urol. 1996;155(4):1191–5.
99. Castilla EA, Liou LS, Abrahams NA, Fergany A, Rybicki LA, Myles J, et al. Prognostic importance of resection margin width after nephron-sparing surgery for renal cell carcinoma. Urology. 2002;60(6): 993–7.
100. Godoy G, Katz DJ, Adamy A, Jamal JE, Bernstein M, Russo P. Routine drain placement after partial nephrectomy is Not always necessary. J Urol Elsevier. 2011;186(2):411–6.
101. Lane BR, Babineau DC, Poggio ED, Weight CJ, Larson BT, Gill IS, et al. Factors predicting renal functional outcome after partial nephrectomy. J Urol. 2008;180(6):2363–8. Discussion 2368–9.
102. Lane BR, Russo P, Uzzo RG, Hernandez AV, Boorjian SA, Thompson RH, et al. Comparison of cold and warm ischemia during partial nephrectomy in 660 solitary kidneys reveals predominant role of nonmodifiable factors in determining ultimate renal function. J Urol. 2011;185(2):421–7.
103. Russo P. Partial nephrectomy for renal cancer (part II): the impact of renal ischaemia, patient preparation, surgical approaches, management of complications and utilization. BJU Int. 2010;105(11):1494–507.
104. Thompson RH, Lane BR, Lohse CM, Leibovich BC, Fergany A, FRANK I, et al. Renal function after partial nephrectomy: effect of warm ischemia relative to quantity and quality of preserved kidney. Urology. 2012;79(2):356–60.
105. Smith GL, Kenney PA, Lee Y, Libertino JA. Nonclamped partial nephrectomy: techniques and surgical outcomes. BJU Int. 2011;107(7):1054–8.
106. Wszolek MF, Kenney PA, Libertino JA. Nonclamping partial nephrectomy: towards improved nephron sparing. Nat Rev Urol. 2011;8(9):523–7.
107. Gill IS, Eisenberg MS, Aron M, Berger A, Ukimura O, Patil MB, et al. "Zero ischemia" partial nephrectomy: novel laparoscopic and robotic technique. Eur Urol. 2011;59(1):128–34.
108. Rais-Bahrami S, George AK, Herati AS, Srinivasan AK, Richstone L, Kavoussi LR. Off-clamp versus complete hilar control laparoscopic partial nephrectomy: comparison by clinical stage. BJU Int. 2012;109(9):1376–81.
109. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC Cancer Staging Manual. 7th ed. Springer; 2009.
110. Crépel M, Jeldres C, Perrotte P, Capitanio U, Isbarn H, Shariat SF, et al. Nephron-sparing surgery is equally effective to radical nephrectomy for T1BN0M0 renal cell carcinoma: a population-based assessment. Urology. 2010;75(2):271–5.
111. Karellas ME, O'Brien MF, Jang TL, Bernstein M, Russo P. Partial nephrectomy for selected renal cortical tumours of ≥ 7 cm. BJU Int. 2010;106(10): 1484–7.
112. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National kidney foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2003;139(2):137–47.