

Chapter 8

Surgical Treatment for Renal Cell Carcinoma

Dae Y. Kim, Jose A. Karam, and Christopher G. Wood

Abstract Systemic therapies for renal cell carcinoma have made modest improvements in patient survival but rarely offer durable cure. Thus, surgical excision of renal cell carcinoma is an integral component of oncologic management. The spectrum of renal cell carcinoma presentation from small renal masses, locally advanced disease, and in the presence of metastasis varies with the surgical armamentarium needed to treat this diverse group of patients. In general for small renal masses, a nephron-sparing approach is preferred if it can be completed safely with negative margins, and for locally advanced tumors, radical nephrectomy is preferred with excision of the affected kidney, lymph nodes, and venous thrombi if present. With metastatic disease, cytoreductive nephrectomy has been shown to prolong survival in carefully selected patients, usually with good performance status and with oligometastasis. The surgical nuances, indication, and motivation for each surgical technique will be discussed in this chapter.

Keywords Kidney cancer • Renal cell carcinoma • Nephrectomy • Partial nephrectomy • Locally advanced kidney cancer • Cytoreductive nephrectomy

8.1 Introduction

The surgical management of kidney disorders was first described by Hippocrates (B.C. 460) where in his works, he mentions “small stones like sand” cause pain and by incising into the kidney the evacuation of pus can be undertaken to relieve the kidney of the abscess and the inciting matter [1]. The first modern surgical removal of the kidney or nephrectomy is credited to Gustav Christoph Jakob Friedrich Ludwig Simon of Germany who performed the first successful procedure on Margaretha Kleb on August 1869. She had a ureteral-vaginal fistula that was unable to be closed on three previous attempts, and a nephrectomy was performed using lumbar access. She was able to leave her bed on day 28 and was discharged after

D.Y. Kim • J.A. Karam • C.G. Wood, MD, FACS (✉)
Department of Urology, MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 1373,
Houston, TX 77030, USA
e-mail: cgwood@mdanderson.org

2 months [2]. Thereafter from 1870–1879, it is documented that 12 nephrectomies for “tumor” were performed with 7 mortalities. Since the first description of the radical nephrectomy, refinements in surgical technique and technological advances have evolved the treatment of the renal mass. Robson et al. in 1969 described a series of 88 patients with removal of the kidney, overlying fat, and regional lymph nodes with 5-year survival rates reported as 66 % when confined to the kidney and 42 % with lymphatic involvement [3]. With nephron-sparing surgery and the introduction of minimally invasive techniques, progressive improvements in patient mortality and morbidity have been observed, heralding the current management of the renal mass. This review will focus on the surgical management of renal cell carcinomas (RCCs) from small renal masses (SRMs) and localized disease to locally advanced and in the setting of metastasis.

The classical presentation of RCC described as flank pain and hematuria with a palpable mass is now uncommon in developed countries with a stated incidence of less than 10 % [4]. A variety of findings may signify RCC, but there is not one pathognomonic finding that defines an RCC diagnosis. Furthermore, the widespread use of cross-sectional abdominal imaging with computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US) has propagated the detection of SRMs that is usually performed for symptoms unrelated to RCC. Currently, most SRMs are discovered incidentally [5] and account for over half of all RCC diagnosis, and while the majority are malignant, between 7 and 33 % have been reported as benign [6]. SRMs are generally defined as ≤ 4 cm, corresponding to tumor stage T1a according to the 2010 TNM staging system for kidney cancer (AJCC) [7]. The distribution of RCC stage at presentation has migrated mainly due to the increased use of cross-sectional imaging, and while the majority are discovered as localized disease, approximately 20 % are stage IV disease [8]. This mixed group of patients require careful risk-benefit counseling as the goals of treatment and complication profile are varied for active surveillance, partial nephrectomy (PN), and radical nephrectomy (RN).

Locally advanced RCCs describe a stage where the tumor may extend beyond the kidney continuously, as with venous thrombus (VT), local nodal involvement, and extension through Gerota’s fascia with or without invasion of adjacent structures. As tumors progress from localized disease to locally advanced and metastatic disease, there may be an increased manifestation of clinical signs and symptoms. For locally advanced disease with VT, lower extremity edema and varicoceles may be present due to obstruction of venous return. It is estimated that 4–10 % of RCC [9] will demonstrate venous involvement in RCC, and the level of VT as a prognostic marker has been controversial [10], motivating the reclassification of the TNM staging system in 2010. The current TNM staging system divides VT level involving the renal vein as T3a, VT within the infradiaphragmatic inferior vena cava (IVC) as T3b, and VT within the supradiaphragmatic IVC or invading the IVC wall as T3c. The 5-year survival is reported as 43.2 %, 37 %, and 22 % for T3a, T3b, and T3c, respectively [11]. The surgical management of locally advanced RCC especially with VT above the diaphragm may require additional surgical

expertise including vascular, hepatobiliary, and cardiothoracic surgeons with bypass to facilitate the safe and complete removal of VT.

It is estimated that as high as one-third of patients will have RCC metastasis at initial presentation and 40 % will have RCC recurrence after treatment of their localized primary [12, 13]. The common sites of RCC metastasis are in the lung, bone, lymph nodes, liver, brain, pancreas, and thyroid [14]. These deposits may manifest symptoms such as seizures and also as pathological fractures for bony involvement. RCC may also secrete endocrine factors causing paraneoplastic syndromes such hypercalcemia and polycythemia and symptoms such as fever and cachexia. The removal of the RCC primary in the setting of metastasis is termed cytoreductive nephrectomy (CN) and has been motivated by two prospective randomized trials demonstrating a survival benefit of CN and interferon-alpha2b versus interferon-alpha2b alone [15, 16]. The selection of patients who would benefit from CN is based on prognostic risk stratification and markers in metastatic RCC (mRCC), details of which are covered in the next chapter. The discovery of metabolic pathways altered in RCC has paved the foundation for therapies that target the vascular endothelial growth factor (VEGF) and the mammalian target of rapamycin (mTOR) pathways. Although objective responses are seen with targeted therapy, complete responses are exceedingly rare, and the management of RCC in the setting of metastasis still remains a surgical disease when feasible.

8.2 Small Renal Masses

Since SRMs are a heterogenous group of benign or pathological masses, the concern for malignancy may motivate further diagnostic imaging, biopsy, and ultimately treatment. In general, SRMs are defined as ≤ 4 cm and confined to the kidney. The benefits of US include the absence of nonionizing radiation, the ability to perform in the office or outpatient setting, and the ability to differentiate between simple cysts and solid, vascular masses – a sign of malignancy. However, further anatomic detail of the tumor landscape is rather limited with US, and CT with contrast is able to characterize the internal enhancement along with details of the vascular anatomy of the kidney. MRI provides similar advantages to CT in providing SRM characterization and the adjacent landscape of structures for the contrast adverse. As many patients with RCC need serial imaging, thereby increasing the potential risk for secondary malignancies, cross-sectioning imaging in the absence of nonionizing radiation may be of benefit.

8.3 Renal Mass Biopsy

The role of renal mass biopsy (RMB) is currently being investigated, and its role in the management of SRM remains controversial. RMB is usually reserved for patients contemplating life-prolonging treatment dictated by the histopathological characterization of the biopsy via targeted therapies, local ablation, and surgical extirpation. In the setting of metastatic disease, RMB will confirm primary RCC versus a nonrenal origin of neoplasm. Patients should have adequate functional status and life expectancy, whereby the benefits of treatment outweigh the risk of RMB. Contemporary series report a low complication rate with risks of bleeding and hematoma, pneumothorax, and pseudoaneurysm formation and the potential risk of needle tract seeding with tumor [17–19]. Several technical points should be considered in RMB such as potential for a nondiagnostic sample with a reported range between 3 and 22 % [20, 21], with marked improvement in diagnostic ability in recent years. Repeat RMB may be advocated or surgical excision can be considered if the ability to obtain a diagnostic sample would be difficult secondary to the location of the mass or if repeat biopsy is considered to be a continued challenge. Another consideration is the diagnostic accuracy of the RMB with the final pathology with accuracies greater than 90 % reported in recent series [22]. In summary, RMB has a low complication rate and should be considered if the biopsy results would radically alter management of the renal mass.

8.4 Management of SRM and Localized RCC

The current management for SRM and localized RCC include (1) active surveillance, (2) partial nephrectomy, (3) radical nephrectomy, and (4) ablation. A broad spectrum of risk and benefit with variable rates of cancer control and cure rates are seen with each option. The natural history of SRMs and the role of active surveillance are covered in the previous chapter. Surgical excision is currently the recommended treatment of choice for localized RCC with partial nephrectomy when technically feasible and radical nephrectomy reserved for larger tumors that are central in location and adjacent to hilar structures, if not amenable to partial nephrectomy. Partial nephrectomy is also recommended for genetic disorders such as von Hippel-Lindau syndrome which predispose to RCC and where repeated surgical treatments are needed. Ablative techniques with various modes of energy, including cryo-, radiofrequency, and microwave ablation, are generally reserved for patients with comorbidities prohibiting or unwilling to undergo surgical removal of the tumor. These techniques are generally performed percutaneously with general and even local anesthesia, best suited for posteriorly located SRMs.

8.4.1 *Partial Nephrectomy*

PN is performed using open, laparoscopic, or robotic techniques. The 10-year metastasis-free estimates have been reported to be greater than 90 % for T1 tumors with both open and laparoscopic approaches [23]. On multivariable analysis, factors associated with metastasis were larger tumor size, an absolute indication for PN, and comorbidity with no significant difference noted between open and laparoscopic PN ($p=0.32$) [23]. The benefit of PN is the preservation of nephrons leading to a decreased risk of renal insufficiency, as renal insufficiency is associated with other secondary morbidity and mortality-causing events. In a retrospective series of 662 patients, the probability of freedom from new-onset renal insufficiency after PN was 80 % versus 35 % after RN with RN identified as an independent risk factor for new-onset renal insufficiency [24]. The renal function outcomes were recently reported for a prospective, randomized study comparing RN and nephron-sparing surgery (NSS) [25]. The estimated glomerular filtration rate (eGFR) <60 for NSS was reached in 64.7 % compared to 85.7 % in RN patients after a median follow-up of 6.7 years.

PN can be performed using a retroperitoneal or transperitoneal approach depending on the location of the tumor and surgeon preference. The technique that is traditionally described for open partial nephrectomy is a flank approach with the patient positioned in the lateral decubitus position or full flank position and an incision extending from the tip of the 11th rib providing safe and adequate exposure to the retroperitoneum. The hilum is dissected, and vascular structures are identified for clamping the artery and/or vein to decrease bleeding during tumor excision. For smaller, exophytic tumors, a clampless technique can be potentially utilized. If the collecting system is entered, absorbable sutures are used to close the collecting system, and figure-of-eight absorbable sutures are used for small vessels. The renorrhaphy is completed by closing the capsule with figure-of-eight absorbable sutures, and dependent on surgeon preference, a hemostatic agent can be applied. Other incisions used in open partial nephrectomy are subcostal, midline, thoracoabdominal, and dorsal lumbotomy approaches which are dictated by tumor location and patient body habitus.

The first laparoscopic PN is credited to Winfield et al. in 1992 in a woman presenting with a calyceal diverticulum and stone [26]. This technique was then first reported for renal tumors by McDougall et al. in 1993 with a wedge resection of an oncocytoma using laparoscopy [27]. Since these initial reports, minimally invasive procedures have shown varied benefit and, in general, have decreased analgesic requirements, less estimated blood loss, and shorter hospital stays while demonstrating similar cancer-specific survival [28, 29]. The context of these benefits must be weighed with the cost-effectiveness and capital investment of minimally invasive approaches along with specialized training and learning curve needed to become adept at approaching complex tumors with equal oncologic control as the open approach.

As for the surgical approach, the patient is positioned in a modified flank position with the camera port placed laterally or through the umbilicus. Working ports are placed in the subcostal area (1) and the other lateral and caudal (2) to the camera port to triangulate around the affected kidney. The assistant ports are placed in the periumbilical area, and a third assistant or laparoscopic/robotic port can be placed either lateral or medial to port 2. The operative steps are similar to the tranperitoneal approach to open PN. The large bowel is reflected medially, and the ureter/gonadal vessel can be used to assist in identifying the hilum. For right-sided tumors, the Kocher maneuver mobilizes the duodenum away from the medial kidney to expose the hilar structures. Ultrasonography is typically used to localize the tumor and mark out the margins for resection. Hilar clamping is performed using laparoscopic bulldogs, and after clamping, the tumor is excised using cold shears. For closure, interrupted figure-of-eight suturing can be used; however, techniques and tools such as Lapra-Tys and the sliding-clip renorrhaphy using hemolock clips have been developed for laparoscopic and robotic surgery to close the excised tumor bed [30, 31]. The developments of these techniques have facilitated decreasing ischemia time and blood loss. Laparoscopic and robotic PN via a retroperitoneal approach has also been described and may be suited for posteriorly located renal tumors or in patients with multiple abdominal surgeries.

8.4.2 Renal Scoring System (Nephrometry)

The variability of tumor location (anterior/posterior, upper/lower pole) and its proximity to hilar structures dictate the anatomic complexity and difficulty in performing a PN. Contemporary scoring and descriptive systems that have been developed to describe these features include mainly the following (Table 8.1): (1) RENAL nephrometry score [32], (2) PADUA classification [33], (3) C-index [34], (4) DAP system [35], and the (5) zonal NePhRO scoring system [36]. The RENAL nephrometry score uses radius of tumor, exo-/endophytic properties, nearness to collecting system/sinus, anterior/posterior location, and location to polar line to quantify a score of complexity as low, medium, and high. The PADUA classification scores tumor size, renal sinus and collecting system involvement, exophytic rate, polar location, and tumor (lateral/medial) rim location. The C-index is a centrality scoring system calculated using the Pythagorean theorem to determine tumor distance to kidney center. The DAP system integrates (D)iameter of tumor, (A)xial distance, and (P)olar distance to report nephrometry. The zonal NePhRO system uses four components, (N)earness to collecting system, (Ph)ysical location (lower, lateral, collecting system location), (R)adius of tumor, and (O)rganization (exo-/endophytic) to describe complexity of renal tumor. Although each nephrometry scoring system measures the anatomic location of kidney tumor to the complexity of excision using its own unique method, validation with clinical variables and survival characteristics is yet to be determined in large multi-institutional cohorts.

Table 8.1 Major renal nephrometry scoring methodologies

System	Variables	1 pt	2 pts	3 pts
RENAL	Radius (maximal diameter)	$R \leq 4$ cm	$4 < R \leq 7$ cm	$R \geq 7$ cm
<i>Low complexity: 4–6</i>	Exo-/endophytic	≥ 50 %	< 50 %	Endophytic
<i>Moderate complexity: 7–9</i>	Nearness to collecting system/sinus	$N \geq 7$ mm	$4 < N < 7$ mm	≤ 4 mm
<i>High complexity: 10–12</i>	Anterior/posterior: a, anterior; p, posterior; x, not determined	–	–	–
h suffix if mass touches the renal artery/vein	Location relative to polar line	Entirely above or below polar line	Crosses polar line	> 50 % of mass is across polar line or mass crosses the axial midline, or mass is between polar line
PADUA	Tumor size	≤ 4 cm	4.1–7 cm	> 7 cm
<i>Low complexity: 6–7</i>	Renal sinus involvement	Not involved	Involved	–
<i>Moderate complexity: 8–9</i>	Collecting system involvement	Not involved	Involved	–
<i>High complexity: ≥ 10</i>	Exophytic rate	≥ 50 %	< 50 %	Endophytic
	Polar location	Superior/inferior	Middle	–
	Tumor rim location	Lateral	Medial	–
DAP	Diameter of tumor	< 2.4 cm	2.4–4.4 cm	> 4.4 cm
	Axial distance	> 1.5 cm	≤ 1.5 cm	Overlap
	Polar distance	> 2 cm	≤ 2 cm	Overlap
Zonal NePhRO	Nearness to collecting system	Mass touches cortex	Mass touches medulla	Mass touches collecting system or crosses renal sinus
<i>Low risk: 4–6</i>	Physical location	Lower pole below collecting system	Lateral to but not touching collecting system	Upper pole or touches collecting system
<i>Intermediate risk: 7–9</i>	Radius of tumor (diameter)	< 2.5 cm	$2.5 \leq R < 4$ cm	≥ 4 cm
<i>High risk: 10–12</i>	Organization (exo-/endophytic)	> 50 % exophytic	50 % endophytic 75 % exophytic	> 75 % endophytic

(continued)

Table 8.1 (continued)

System	Variables	1 pt	2 pts	3 pts
C-index score:	Centrality index scoring	No point system but calculation of centrality index by the following:		
<i>0 = mass concentric to kidney center</i>		Cross-sectional imaging and Pythagorean theorem to calculate distance from tumor center to kidney center. Division with tumor size to obtain centrality index		
<i>1 = periphery touching kidney center</i>				
<i>Larger index = increased distance to kidney center</i>				

8.4.3 Radical Nephrectomy

Complete excision by PN is preferred for SRMs in healthy individuals. In 2009, the American Urological Association (AUA) presented guidelines for clinical T1 renal masses listing radical nephrectomy (RN) as a viable treatment option for patients where PN is not technically feasible. In a multi-institutional study (EORTC 30904) [29], patients randomized to either nephron-sparing surgery (NSS) or RN for renal tumors ≤ 5 cm showed that the 10-year overall survival (OS) was 75.7 % for NSS compared to 81.1 % for RN ($p =$ not significant). The 10-year progression rate for NSS was 4.1 % and for RN was 3.3 % ($p = 0.48$). The NSS group had a slightly higher rate of complications with pleural and splenic injury, bleeding, and urine leaks. Approximately 85.7 % of patients who underwent RN had renal dysfunction with an estimated glomerular filtration rate (eGFR) < 60 , compared to 64.7 % of patients after NSS at a median follow-up of 6.7 years. For advanced kidney disease (defined as eGFR < 30), 10 % of RN and 6.3 % of NSS patients reached this point, and about 2 % of patients in each group demonstrated extreme renal dysfunction (eGFR < 15). Thus, the decreased moderate renal dysfunction seen with NSS did not demonstrate a survival benefit in this group of patients for this follow-up time period.

The removal of the whole kidney for a peripherally located/exophytic SRM theoretically seems to remove an excess amount of normal kidney parenchyma unnecessarily. The surgeon should consider patient age and comorbidities, life expectancy, and oncologic goals of treatment when considering RN versus a nephron-sparing approach. Although, EORTC 30904 did not demonstrate a survival benefit in patients with clinical T1 masses who had NSS during follow-up, the higher rates of moderate renal dysfunction in RN patients may increase progressive renal insufficiency requiring dialysis along with its associated risk factors such as cardiovascular events after longer follow-up time periods [24, 25]. From a technical

approach, RN for SRMs can be performed by laparoscopic or open surgery with similar steps as described above for PN with hilar vessel control and division. In general, RN should be reserved for masses whereby NSS is not easily possible and where the expeditious removal of the kidney facilitates recovery in patients with marginal surgical candidacy.

8.5 Locally Advanced Disease

Surgical excision of locally advanced RCC requires careful planning, patient optimization, and coordination of medical specialists and urologic surgeons. As in SRMs, the oncologic goals of locally advanced RCC are identical, to provide the greatest survival benefit with palliation of clinical symptoms, with the lowest morbidity possible. The definition of locally advanced RCC is typically defined as $\geq T3$ in the absence of distant metastasis [37]. For the surgical excision of RCC with concomitant thrombectomy in M0 (nonmetastatic) patients, the reported median survival range from 35 to 116 months with the 5-year CSS ranging between 40 and 65 % [38, 39]. For metastatic and T4 disease, the 5-year CSS is significantly lower ranging between 6.5 and 19 % [39, 40]. In comparison, the natural course or untreated RCC with VT is rather dismal with a recent Surveillance, Epidemiology, and End Results (SEER) database study reporting a median survival time of 5 months and a 1-year DSS as 29 % [41]. In this study, patients are of advanced stage and of poor performance status prohibiting primary surgical treatment. However, a subset analysis of nodal and metastasis-free (N0, M0) patients in this study demonstrate a significantly longer median survival of 14 months. Thus, the complete excision of RCC with concomitant VT removal may significantly increase survival [42].

The surgical excision of locally advanced RCC is more invasive compared to techniques developed for SRMs with surgical maneuvers performed to optimize exposure and removal. Due to the varying scope of locally advanced RCC, open, laparoscopic, and robotic techniques have been described with transabdominal and retroperitoneal approaches with different types of surgical incisions such as midline, subcostal/bilateral chevron, flank, and thoracoabdominal incisions. The midline incision allows exposure to the affected renal hilum as well as the contralateral renal vasculature and when extended to the thorax, the retrohepatic inferior vena cava, and the cardiac vasculature. Similar exposure can be obtained with bilateral chevron with an extended midline/thorax incision and with a flank incision extended to the thorax (a thoracoabdominal incision). Hepatic mobility may be facilitated by transection of the left triangular and coronary ligaments to provide exposure to the retrohepatic IVC.

The surgical steps for excision of RCC with associated venous thrombus (VT) include the isolation of the renal hilum with control of the renal artery first. The renal vein, IVC, and the contralateral renal vein are isolated and sequentially clamped cephalad and caudal to the VT. The VT can be visualized and monitored

for extraction using transesophageal echocardiography. The VT is extracted with a cavotomy en bloc with the affected renal vein. The IVC can then be reconstructed primarily, or if the diameter is less than 50 % of the original diameter, a graft can be utilized. The VT may also directly invade the IVC; in this instance, the IVC may be removed en bloc with reconstruction using vascular grafts as needed. For VT above the diaphragm and into the cardiac vasculature, cardiopulmonary (CPB) and venovenous (VVB) bypass may be used to facilitate VT removal. In general, VVB is not used for VT involving the right atrium and, due to the shorter bypass circuit, may provide shorter operative times compared to CPB.

8.6 Lymphadenectomy

The EORTC 30881 was a randomized trial examining therapeutic benefit of RN with and without lymph node dissection (LND) [43]. A total of 772 patients were selected for randomization with 383 patients in the LND group and 389 in the non-LND group. The majority (~70 %) of these patients were of lower-stage tumors ($\leq T2$). Pathological analysis of the LND dissections revealed an absence of LN metastasis in 332 patients out of 346 (96 %). Palpably enlarged LNs during surgery did not demonstrate LN metastasis as the majority (80 %) were negative and only 1 % with non-palpable nodes were positive. In the patients that did not undergo a LND, 9 % of patients had enlarged LNs. These LNs were excised for staging purposes or biopsied with 12 % demonstrating LN metastasis. In all, 96 % of the resected group did not show LN metastasis, and there were no significant differences in all survival parameters (overall, time to progression, or progression-free survival) at a median follow-up period of 12.6 years. The main criticism of this study was that the majority of patients were of low-risk disease, and benefits of a formal LND would not demonstrate much of a survival benefit.

LND may be of limited benefit for low-stage renal tumors as noted previously. On the contrary, it is hypothesized that LND may benefit higher-stage tumors and/or renal tumors with adverse pathological features. As retrospective studies have shown LN metastasis to be stage dependent ranging between 12 and 37 % for T3–4 tumors [44, 45]. At our institution, the borders of a formal LND are ipsilateral hilar LNs and para-aortic LNs from the crus of the diaphragm to the aortic bifurcation for left-sided tumors. For right-sided tumors, the interaortocaval and para-caval LNs are removed from the crus of the diaphragm to the large vessel bifurcation [46].

8.7 Cytoreductive Nephrectomy

Approximately 25 % of RCC patients will initially present with metastatic disease with treatments mainly focused on systemic therapies [47]. In 2001, two phase III randomized clinical trials reported a statistically significant survival benefit when radical nephrectomy was combined with interferon-alpha2b. In EORTC 30947 [16], 42 participants were randomly assigned to the RN before interferon-alpha2b and 43 to the interferon-alpha2b alone. The time to progression was 5 months versus 3 months (HR 0.60, 95 % CI 0.36–0.97) and median survival of 17 versus 7 months (HR 0.54, 95 % CI 0.31–0.94) with favorable survival observed when combined with RN. The Southwest Oncology Group (SWOG) randomized 121 to interferon alone versus 120 to RN plus interferon-alpha2b [15]. When combined with surgery, there was a 3-month ($P = 0.05$) improvement in median survival (11.1 vs. 8.1 months), independent of performance status and site of metastatic spread.

Although these two trials used immunotherapies, they have continued to motivate cytoreductive nephrectomy (CN) in the contemporary targeted therapy era. Targeted agents such as the tyrosine kinase inhibitors (sorafenib, sunitinib, and axitinib), mTOR inhibitors, and VEGF antibodies have been explored as agents used after CN [48–53]. These studies examined CN in subgroup analysis with the primary end point of progression-free survival to show promising trends in survival improvement. There are two ongoing randomized trials accruing to examine CN with targeted therapies. The EORTC 30073 (SURTIME trial, NCT 01099423) is a randomized phase III trial comparing immediate versus delayed (after receiving two cycles of sunitinib) nephrectomy in patients with synchronous metastatic RCC. The trial is still accruing with an expected enrollment of 458 patients. The CARMENA trial (NCT 00930033) randomizes to RN and sunitinib versus sunitinib alone with the primary end point of overall survival. The estimated accrual is 576 patients. It is expected that the results of these two trials will refine the role and timing of CN with targeted agents.

8.8 Conclusion

The spectrum of renal masses from SRMs to locally advanced and metastatic disease varies the management from active surveillance to invasive procedures including surgery. Due to the variability in biology and relative resistance to systemic therapies of RCC, surgery remains an important component of treatment. Since the first modern description of radical nephrectomy for tumor was described in the late 1800s, refinements in surgical technique have evolved to remove the kidney, perinephric fat, and regional lymph nodes for primary oncologic control. With partial nephrectomy, the removal of the whole kidney is not necessary for SRMs, and the development of laparoscopy and robotic techniques have advanced the treatment paradigm. As patients present in different stages of disease each with

their own unique clinical factors, informed counseling is paramount to meet their expectations. Furthermore, as many treatment methodologies are based on retrospective and observational studies, enrollment in clinical trials should be encouraged. As we await the conclusion of current trials with the introduction of new systemic therapies, the role of surgical excision is evolving.

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