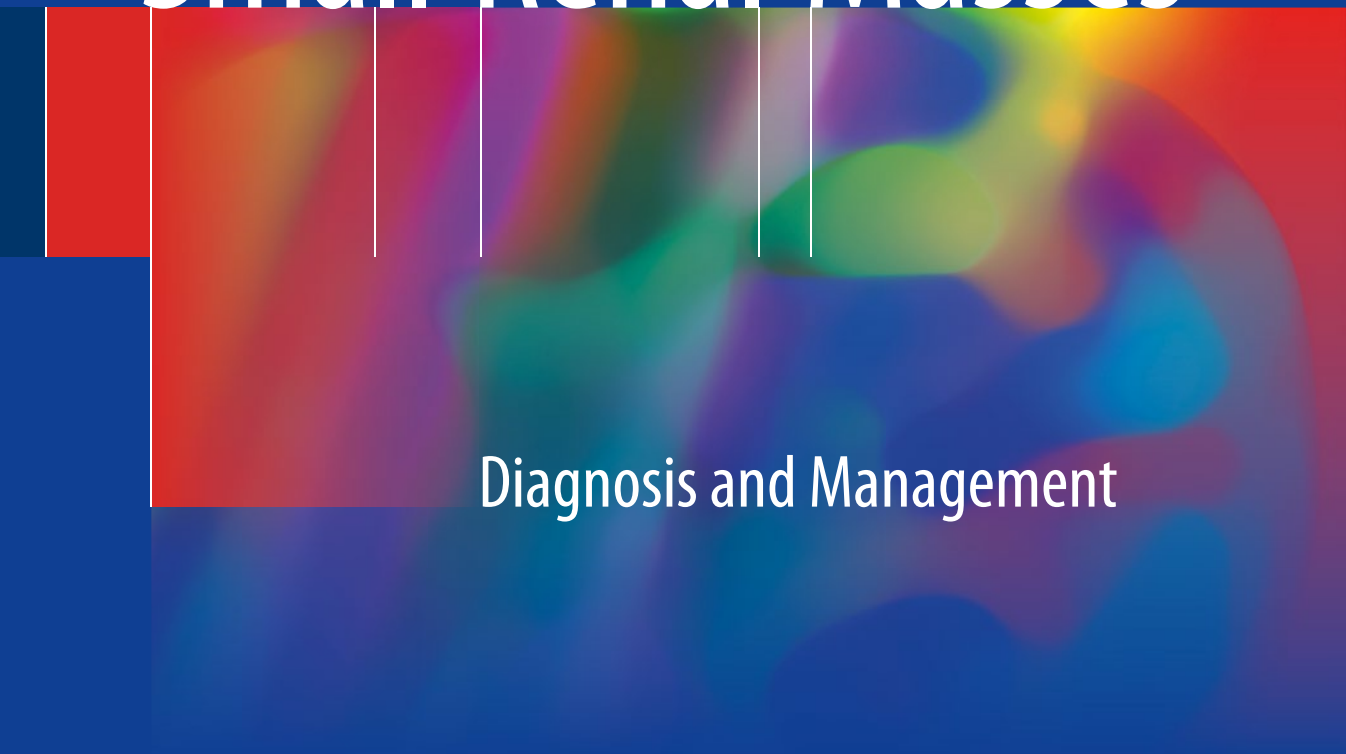
Kamran Ahmed · Nicholas Raison
Ben Challacombe · Alexandre Mottrie
Prokar Dasgupta *Editors*

The Management of Small Renal Masses



Diagnosis and Management

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Foreword

The advent of modern imaging has brought about detection of renal cancer in the earliest of stages. Small renal masses account for the majority of kidney lesions detected today. This along with a better understanding of disease biology and technological developments has changed the way renal cancer is treated.

Up until now, there has been no single exhaustive reference on the management of our new age of renal cancer. Dr. Dasgupta and colleagues need to be commended for assembling this comprehensive text on managing small renal masses. The entire spectrum of management is reviewed with chapters addressing the latest in diagnosis as well as treatment. Surveillance is becoming much more prevalent, and the text does an outstanding job in outlining paradigms for safe conservative management. Indications for interventional approaches are laid out clearly allowing students of surgery to understand the rationale for each modality.

Technical detail in both surgical and interventional treatments is more than complete giving step-by-step approaches that include laparoscopic, open, robotic, and ablative modalities. Results of intervention are very well reviewed, and schema for a long-term follow-up are lucidly outlined.

Finally, no comprehensive review would be complete without a review of complications. The core of understanding is achieved when one understands how to preempt or manage a catastrophe. These issues are covered deftly and thoroughly.

In conclusion, I again praise the editors for producing this important and much-needed opus on managing renal masses. I can unequivocally say this is a “must-read” for all those who manage these patients.

New York, NY, USA — Louis R. Kavoussi, M.D., M.B.A.

Contents

Renal Anatomy and Physiology

1

Nicolòmaria Buffi, Pasquale Cardone, and Giovanni Lughezzani

Key Messages

1. The kidney is divided into the cortex and medulla. The medullary areas are pyramidal, more centrally located, and separated by sections of cortex. These segments of cortex are called the columns of Bertin.
2. Gerota's fascia can be considered as an anatomic barrier to the spread of malignancy and a means of containing perinephric fluid collections.
3. From anterior to posterior, the renal hilar structures are the renal vein, renal artery, and collecting system.
4. The progression of arterial supply to the kidney is as follows: renal artery → segmental artery → interlobar artery → arcuate artery → interlobular artery → afferent artery.
5. Each renal pyramid terminates centrally in a papilla. Each papilla is cupped by a minor calyx. A group of minor calyces join to form a major calyx. The major calyces combine to form the renal pelvis.

1.1 Macroscopic and Microscopic Anatomy of the Kidney

Grossly, the kidneys are bilaterally paired reddish-brown organs. Typically each kidney weighs 150 g in the male and 135 g in the female. The kidneys generally measure 10–12 cm vertically, 5–7 cm transversely, and 3 cm in the anteroposterior dimension (Fig. 1.1). Because of compression by the liver, the right kidney tends to be somewhat shorter and wider. In children, the kidneys are relatively larger and possess more

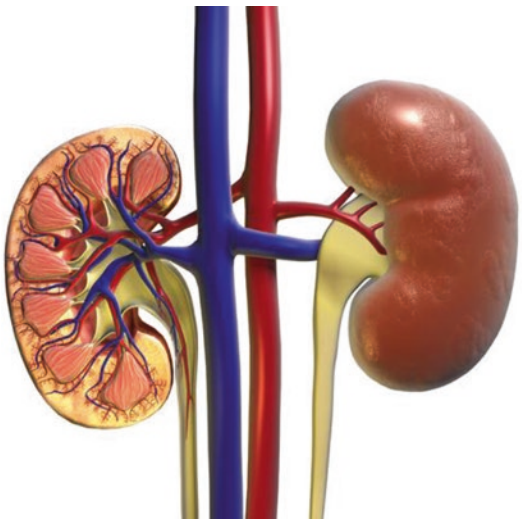

Fig. 1.1 Relative position of the left and right kidney and renal vessels

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prominent foetal lobulations. These lobulations are present at birth and generally disappear by the first year of life, although occasionally they persist into adulthood. An additional common feature of the gross renal anatomy is a focal renal parenchymal bulge along the kidney's lateral contour, known as a dromedary hump. This is a normal variation without pathologic significance. It is more common on the left than the right and is believed to be caused by downward pressure from the spleen or liver. As one proceeds centrally from the peripherally located reddish-brown parenchyma of the kidney, the renal sinus is encountered. Here the vascular structures and collecting system coalesce before exiting the kidney medially. These structures are surrounded by yellow sinus fat, which provides an easily recognized landmark during renal procedures such as partial nephrectomy. At its medial border, the renal sinus narrows to form the renal hilum. It is through the hilum that the renal artery, renal vein, and renal pelvis exit the kidney and proceed to their respective destinations. Both grossly and microscopically, there are two distinct components within the renal parenchyma: the inner medulla and outer cortex. Unlike the adrenal gland, the renal medulla is not a contiguous layer. Instead, the medulla is composed of multiple, distinct, conically shaped areas noticeably darker in colour than the cortex. These same structures are also commonly called renal pyramids, making the terms renal medulla and renal pyramid synonymous. The apex of the pyramid is the renal papilla, and each papilla is cupped by an individual minor calyx. The renal cortex is lighter in colour than the medulla and not only covers the renal pyramids peripherally but also extends between the pyramids themselves. The extensions of cortex between the renal pyramids are given a specific name: the columns of Bertin. These columns are particularly important during surgical procedures because it is through these columns that renal vessels traverse from the renal sinus to the peripheral cortex, decreasing in diameter as the columns move peripherally. It is because of this anatomy that percutaneous access to the collecting system is made through a renal pyramid into a calyx, thus avoiding the columns of Bertin and the larger vessels found within them (Fig. 1.2).

The position of the kidney within the retroperitoneum varies greatly by side, degree of inspiration, body position, and presence of anatomical anomalies. The right kidney sits 1–2 cm lower

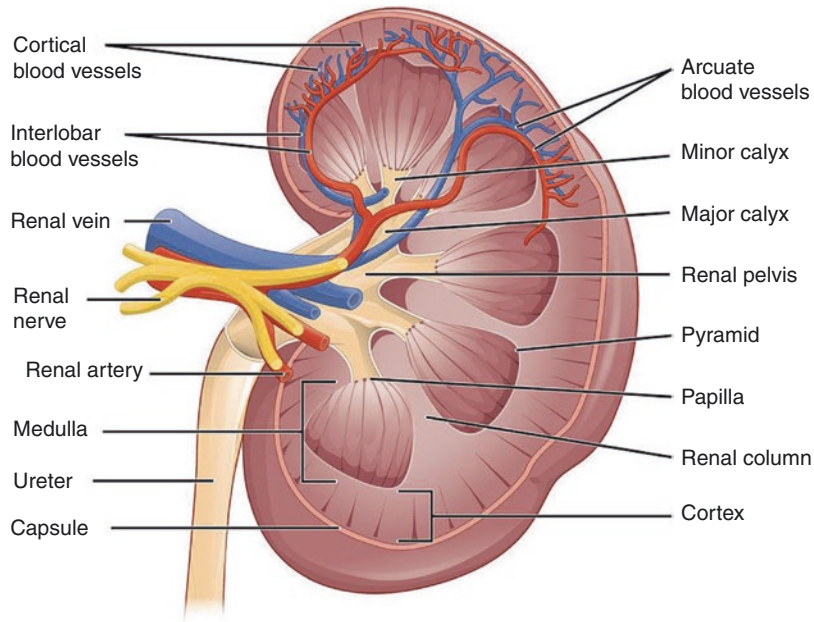

Fig. 1.2 Gross internal anatomy of the kidney

than the left in most individuals owing to displacement by the liver. Generally, the right kidney resides in the space between the top of the first lumbar vertebra to the bottom of the third lumbar vertebra. The left kidney occupies a more superior space from the body of the twelfth thoracic vertebral body to the third lumbar vertebra. Of surgical importance are the structures surrounding the kidney. Interposed between the kidney and its surrounding structures is the perirenal or Gerota's fascia. This fascial layer encompasses the perirenal fat and kidney and encloses the kidney on three sides: superiorly, medially, and laterally. Superiorly and laterally, Gerota's fascia is closed, but medially it extends across the midline to fuse with the contralateral side. Inferiorly, Gerota's fascia is not closed and remains an open potential space. Gerota's fascia can be considered as an anatomic barrier to the spread of malignancy and a means of containing perinephric fluid collections. Hence, perinephric fluid collections can track inferiorly into the pelvis without violating Gerota's fascia. Both kidneys have similar muscular surroundings. Posteriorly, the diaphragm covers the upper third of each kidney, with the 12th rib crossing at the lower extent of the diaphragm. Important to note for percutaneous renal procedures and flank incisions is that the pleura extends to the level of the 12th rib posteriorly. Medially the lower two thirds of the kidney lie against the psoas muscle, and laterally the quadratus lumborum and aponeurosis of the transversus abdominis muscle are encountered. First, the lower pole of the kidney lies laterally and anteriorly relative to the upper pole. Second, the medial aspect of each kidney is rotated anteriorly at an angle of approximately 30°. An understanding of this renal orientation is again of particular interest for percutaneous renal procedures in which kidney orientation influences access site selection. Anteriorly, the right kidney is bordered by a number of structures. Cranially, the upper pole lies against the liver and is separated from the liver by the peritoneum except for the liver's posterior bare spot. The hepatorenal ligament further attaches the right kidney to the liver because this extension of parietal peritoneum bridges the upper pole of the right kidney to the posterior liver. Also at the upper pole, the right adrenal gland is encountered. On the medial aspect, the descending duodenum is intimately related to the medial aspect of the kidney and hilar structures. Finally, on the anterior aspect of the lower pole lies the hepatic flexure of the colon. The left kidney is bordered superiorly by the tail of the pancreas with the splenic vessels adjacent to the hilum and upper pole of the left kidney. The left adrenal gland is also found cranial to the upper pole and further, superolaterally, the spleen. The splenorenal ligament attaches the left kidney to the spleen. This attachment can lead to splenic capsular tears if excessive downward pressure is applied to the left kidney. Superior to the pancreatic tail, the posterior gastric wall can overlie the kidney. Caudally, the kidney is covered by the splenic flexure of the colon.

The renal excretory system consists of papillae, calyces, and the renal pelvis. The renal papillae are the tip of a medullary pyramid and constitute the first gross structure of the collecting system. Typically, there are seven to nine papillae per kidney, but this number is variable, ranging from 4 to 18. The papillae are aligned in two longitudinal rows situated approximately 90° from one another. There is an anterior row that, owing to the orientation of the kidney, faces in a lateral direction and a posterior row that extends directly posterior. Each of these papillae is cupped by a minor calyx. In the upper and lower poles, compound calyces are often encountered. These compound calyces are the result of renal pyramid fusion and because of their anatomy are more likely to allow reflux into the renal parenchyma. Clinically this can result in more severe scarring of the parenchyma overlying compound calyces. After cupping an individual papilla, each minor calyx narrows to an infundibulum. Just as there is frequent variation in the number of calyces, the diameter and length of the infundibula vary greatly. Infundibula combine to form two or three major calyceal branches. These are frequently termed the upper, middle, and lower pole calyces, and the calyces in turn combine to form the renal pelvis. The renal pelvis itself can vary greatly in size, ranging from a small intrarenal pelvis to a large predominantly extrarenal pelvis. Eventually the pelvis narrows to form the ureteropelvic junction, marking the beginning of

the ureter. On close examination, it is clear that there is significant variation in the anatomy of the renal collecting system with the number of calyces, diameter of the infundibula, and size of the renal pelvis all varying significantly amongst normal individuals. Even in the same individual, the renal collecting systems may be similar but are rarely identical. Microscopically, the renal collecting system originates in the renal cortex at the glomerulus where filtrate enters the Bowman's capsule. Together the glomerular capillary network and Bowman's capsule form the renal corpuscle (Malpighian corpuscle). The glomerular capillary network is covered by specialized epithelial cells called podocytes that, along with the capillary epithelium, form a selective barrier across which the urinary filtrate must pass. The filtrate is initially collected in Bowman's capsule and then moves to the proximal convoluted tubule. The proximal tubule is composed of a thick cuboidal epithelium covered by dense microvilli. These microvilli greatly increase the surface area of the proximal tubule, allowing a large portion of the urinary filtrate to be reabsorbed in this section of the nephron. The proximal tubule continues deeper into the cortical tissue where it becomes the loop of Henle. The loop of Henle extends variable distances into the renal medulla. Within the renal medulla, the loop of Henle reverses course and moves back toward the periphery of the kidney. As it ascends out of the medulla, the loop thickens and becomes the distal convoluted tubule. This tubule eventually returns to a position adjacent to the originating glomerulus and proximal convoluted tubule. Here the distal convoluted tubule turns once again for the interior of the kidney and becomes a collecting tubule. Collecting tubules from multiple nephrons combine into a collecting duct that extends inward through the renal medulla and eventually empties into the apex of the medullary pyramid, the renal papilla.

1.2 Renal Vasculature

The renal pedicle classically consists of a single artery and a single vein that enter the kidney via the renal hilum. These structures branch from the aorta and inferior vena cava just below the superior mesenteric artery at the level of the second lumbar vertebra. The vein is anterior to the artery. The renal pelvis and ureter are located posteriorly to these vascular structures. The right renal artery leaves the aorta and progresses with a caudal slope under the inferior cava vein toward the right kidney. The left renal artery courses horizontally, directly to the left kidney. Given the rotational axis of the kidney, both renal arteries move posteriorly as they enter the kidney. Both arteries also have branches supplying their respective adrenal gland, renal pelvis, and ureter. Approaching the kidney, the renal artery divides into four or more branches (most commonly five). These are the renal segmental arteries. Each segmental artery supplies a distinct portion of the kidney with no collateral circulation between them. Thus, occlusion or injury to a segmental branch will cause segmental renal infarction. Generally, the first and most constant branch is the posterior segmental branch, which separates from the renal artery before it enters the renal hilum. Typically, there are four anterior branches, which from superior to inferior are apical, upper, middle, and lower. The relationship of these segmental arteries is important because the posterior segmental branch passes posterior to the renal pelvis, while the others pass anterior to the renal pelvis. Ureteropelvic junction obstruction caused by a crossing vessel can occur when the posterior segmental branch passes anterior to the ureter causing occlusion. This division between the posterior and anterior segmental arteries has an additional surgical importance since between these two circulations is an avascular plane. This longitudinal plane lies just posterior to the lateral aspect of the kidney. Incision within this plane results in significantly less blood loss than outside it. However, there is significant variation in the location of this plane, requiring careful delineation before incision. This can be done with either preoperative angiography or intraoperative segmental arterial injection with a dye such as methylene blue. Once in the renal sinus, the segmental arteries branch into lobar arteries, which further subdivide within the renal parenchyma to form interlobar arteries. These interlobar arteries

progress peripherally within the cortical columns of Bertin, thus avoiding the renal pyramids but maintaining a close association with the minor calyceal infundibula. At the base (peripheral edge) of the renal pyramids, the interlobar arteries branch into arcuate arteries. Instead of moving peripherally, the arcuate arteries run parallel with the edge of the corticomedullary junction. Interlobular arteries branch off the arcuate arteries and move radially, where they eventually divide to form the afferent arteries to the glomeruli.

The two million glomeruli within each kidney represent the core of the renal filtration process. Each glomerulus is fed by an afferent arteriole. As blood flows through the glomerular capillaries, the urinary filtrate leaves the arterial system and is collected in the glomerular (Bowman's) capsule. Blood flow leaves the glomerular capillary via the efferent arteriole and continues to one of two locations: secondary capillary networks around the urinary tubules in the cortex or descending into the renal medulla as the vasa recta. The renal venous drainage correlates closely with the arterial supply. The interlobular veins drain the postglomerular capillaries. These veins also communicate freely via a subcapsular venous plexus of stellate veins with veins in the perinephric fat. After the interlobular veins, the venous drainage progresses through the arcuate, interlobar, lobar, and segmental branches, with the course of each of these branches mirroring the corresponding artery. After the segmental branches, the venous drainage coalesces into three to five venous trunks that eventually combine to form the renal vein. Unlike the arterial supply, the renal veins communicate freely, forming venous collars around the infundibula. This creates an extensive collateral circulation in the venous drainage of the kidney. Surgically, this is important because unlike the arterial supply, occlusion of a segmental venous branch has little effect on venous outflow. The renal vein is located directly anterior to the renal artery, although this position can vary up to 1–2 cm cranially or caudally relative to the artery. The right renal vein is generally 2–4 cm in length and enters the right lateral to posterolateral edge of the inferior cava vein. The left renal vein is typically 6–10 cm in length and enters the left lateral aspect of the inferior cava vein after passing posterior to the superior mesenteric artery and anterior to the aorta. Compared with the right renal vein, the left renal vein enters the inferior cava vein at a slightly more cranial level and a more anterolateral location. Additionally, the left renal vein receives the left adrenal vein superiorly, lumbar vein posteriorly, and left gonadal vein inferiorly. The right renal vein typically does not receive any branches.

1.3 Renal Lymphatics and Nervous Innervation

The renal lymphatics largely follow blood vessels through the columns of Bertin and then form several large lymphatic trunks within the renal sinus. As these lymphatics exit the hilum, branches from the renal capsule, perinephric tissues, renal pelvis, and upper ureter drain into these lymphatic vessels. They then empty into lymph nodes associated with the renal vein near the renal hilum. From here, the lymphatic drainage between the two kidneys varies.

On the left, primary lymphatic drainage is into the left lateral para-aortic lymph nodes including nodes anterior and posterior to the aorta between the inferior mesenteric artery and the diaphragm. Occasionally, there will be additional drainage from the left kidney into the retrocrural nodes or directly into the thoracic duct above the diaphragm. On the right, drainage is into the right inter-aortocaval and right paracaval lymph nodes including nodes located anterior and posterior to the vena cava, extending from the common iliac vessels to the diaphragm. Occasionally, there will be additional drainage from the right kidney into the retrocrural nodes or the left lateral para-aortic lymph nodes.

Innervation of the sympathetic preganglionic nerves originates from the eighth thoracic through to the first lumbar spinal segments and then travels to the coeliac and aorticorenal ganglia. From here, postganglionic fibres travel to the kidney via the autonomic plexus surrounding

the renal artery. Parasympathetic fibres originate from the vagus nerve and travel with the sympathetic fibres to the autonomic plexus along the renal artery. The primary function of the renal autonomic innervation is vasomotor, with the sympathetics inducing vasoconstriction and the parasympathetics causing vasodilation. Despite this innervation, it is important to realize that the kidney functions well even without this neurologic control, as evidenced by the successful function of transplanted kidneys.

Introduction to T1 Renal Tumours and Prognostic Indicators

2

Vincenzo Ficarra, Marta Rossanese, Alessandro Crestani, Gioacchino De Giorgi, Guido Martignoni, and Gianluca Giannarini

Abbreviations

ARCD	Acquired renal cystic disease
CSS	Cancer-specific survival
ESRD	End-stage renal disease
NSS	Nephron-sparing surgery
OS	Overall survival
PN	Partial nephrectomy
RCC	Renal cell carcinoma
UCS	Urinary collecting system
VHL	von Hippel-Lindau

Key Messages

1. Kidney cancers represent the 14th most common malignancies with more than 300,000 new cases diagnosed in 2012.
2. In 2012, kidney cancers accounted for 143,000 deaths with a crude rate value of 2% of all cancer deaths.
3. Cigarette smoking, overweight and obesity and arterial hypertension are the most prevalent modifiable risk factors for RCC in both genders.
4. Preoperative variables influencing the decision-making process for T1 renal tumours can be classified as patient-related (age, co-morbidities and performance status) and tumour-related (mode of presentation, clinical tumour size and anatomical/topographic characteristics) factors.
5. The use of nephrometry systems (RENAL or PADUA) to define the anatomical and topographic characteristics of small renal masses should be considered the standard of care for the preoperative evaluation of patients suitable to nephron-sparing surgery.
6. Treatment of cT1N0M0 parenchymal renal tumours should be based on patient-related factors, tumour-related characteristics and surgeon experience.

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7. Beyond tumour characterization according to histological subtype, the most important traditional pathological factors dictating the prognosis of patients with RCCs are the pathological size and extent of the primary tumour, nuclear grading, coagulative necrosis, microvascular invasion and sarcomatoid dedifferentiation.
8. Prognosis can be estimated combining clinical and pathological factors in the context of mathematical models. This information can be used to improve the counselling process and to guide the follow-up.

2.1 Epidemiology and Aetiology

Kidney cancers represent the 14th most common malignancies with more than 300,000 new cases diagnosed in 2012. Renal cell carcinoma (RCC) accounts for approximately 90% of all kidney cancers. According to the gender, around 200,000 new cases were observed in men and 100,000 in women. Moreover, there were around 198,000 new cases in more developed regions and 130,000 in less developed regions [1]. Indeed, renal tumours are more frequently detected in Europe, North America and Australia than in India, Japan, Africa and China. The Czech Republic, Lithuania, Latvia, Estonia and Iceland have the highest incidence in Europe. Interestingly, the incidence of kidney cancers is declining in some European countries, namely, Sweden, Poland, Finland and the Netherlands [2]. Furthermore, incidence rates in Europe and the USA increase consistently with age. This trend can be strongly correlated with the parallel use of non-invasive diagnostic testing, such as abdominal ultrasound, for symptoms that are not strictly related to the suspicion of kidney cancer.

In 2012, kidney cancers accounted for 143,000 deaths with a crude rate value of 2% of all cancer deaths. 91,000 deaths were in men (crude rate 2.6%) and 52,000 in women (crude rate 1.5%) [1]. Like incidence trends, overall mortality rates were highest in North America, Australia/New Zealand and Europe and lowest in Africa and Asia [2]. After several years of increasing trends in RCC mortality, it seems that rates are stabilizing or even declining in many Western countries. In Europe, a decrease in mortality was observed in Scandinavian countries, France, Germany, Italy, Austria and the Netherlands, while increased mortality rates are still reported in Ireland and Slovenia [2].

Cigarette smoking, being overweight and obese and arterial hypertension are the most prevalent modifiable risk factors for RCC in both genders. Thus, recommended strategies to prevent kidney cancers should entail programmes for smoking cessation, reducing excess body weight and treatment of uncontrolled arterial blood pressure. Notably, patients with end-stage renal disease (ESRD) or on long-term haemodialysis developing an acquired renal cystic disease (ARCD) present a significant risk to develop RCC. Therefore, these patients should be regularly screened. On the other hand, it is unclear whether renal transplantation in these patients can reduce the risk to develop RCC [3].

Numerous studies have tested the potential role of nutrition and diet as risk factors for RCC. Conflicting or inconclusive data have been reported for proteins and fats, vitamins, fruits and vegetables, meat and fish, alcohol, coffee and other beverages. Currently no dietary recommendations can be given. Moreover, epidemiological studies have demonstrated that kidney cancer should not be considered to be a typical occupation-related tumour. Nevertheless, current guidelines recommend decreasing or preventing exposure to occupational carcinogens like asbestos, polycyclic aromatic hydrocarbons, dry-cleaning solvents and cadmium [2].

Genetic factors are implicated in the development of the 2–3% of familial RCC syndromes, such as von Hippel-Lindau syndrome, hereditary papillary RCC syndrome, familial leiomyomatosis and RCC syndrome and Birt-Hogg-Dubè syndrome. All these syndromes are transmitted in an autosomal-dominant manner. Germline mutations in the von Hippel-Lindau (VHL) gene are

the most common alterations, and active screening in these patients might be considered to detect RCC at an early enough stage to permit nephron-sparing surgery (NSS).

Despite advances in imaging techniques and the increase in incidentally detected renal tumours with abdominal ultrasound performed for unrelated complaints, about 20–30% of all patients are still diagnosed with metastatic disease. Moreover, 20–30% of patients undergoing surgical treatments for organ-confined disease will have a local relapse or develop distant metastases [2]. This chapter focuses on non-metastatic RCC confined to the parenchyma and ≤7 cm in largest size, i.e. clinically T1N0M0. The 2009 TNM staging system classifies organ-confined renal tumours according to the 7-cm size cut-off. Specifically, masses ≤7 cm are classified as T1 and larger tumours as T2. Moreover, the latest version of TNM classification confirms the classical stratification of T1 tumours in two different subgroups (T1a and T1b) according to the 4-cm size cut-off. Notably, the system introduces a further stratification of T2 tumours in two categories (T2a and T2b), according to the 10-cm size cut-off [4].

Several clinical factors play a relevant role in the decision-making process for surgical treatment planning of T1N0M0 RCC. Similarly, certain pathological features warrant tailored post-operative management plan and, in the future, will determine selection for targeted adjuvant therapy. Moreover, both clinical and pathological factors are key to predicting the prognosis of patients who are candidates for surgical treatment. To improve their accuracy, prognostic variables have been combined to generate mathematical models, such as algorithms and nomograms [4].

2.2 Clinical Factors

Preoperative variables influencing the decision-making process for T1 renal tumours can be classified in patient-related (age, co-morbidities and performance status) and tumour-related (mode of presentation, clinical tumour size and anatomical/topographic characteristics) factors.

Few data are available about the potential impact of age on renal tumour characteristics and prognosis. A multi-institutional study showed that patients aged ≤40 years were more likely to have papillary or chromophobe RCC and less likely to have clear cell RCC. Interestingly, the authors have observed that age was an independent predictor of cancer-specific survival (CSS), with older patients having significantly worse survival [5]. Notably, Sun et al. recently published a SEER database analysis showing that in patients aged ≥75 years, 2- and 5-year overall survival (OS) is comparable after radical nephrectomy or partial nephrectomy (PN). According to this study, the indication for elective PN in patients aged ≥75 years should be carefully discussed during pretreatment counselling [7]. Similar considerations can be made considering the co-morbidity profile of patients with T1 tumours suitable for NSS. Indeed, in the SEER registry analysis, patients with >2 baseline co-morbidities showed a comparable 2- and 5-year OS after PN or radical nephrectomy [7]. Therefore, patient co-morbidities must be taken into account as a selection criterion for NSS. Performance status was an independent predictor of CSS [7], but its prognostic role seems to be more relevant in patients with locally advanced or metastatic tumours [8].

Considering preoperative tumour-related variables, mode of presentation was extensively evaluated, and its independent predictive role was demonstrated in multi-institutional series [8]. According to the Patard classification, tumours diagnosed during abdominal imaging for signs and symptoms unrelated to RCC are classified as incidental (S1). Conversely, flank pain, haematuria and flank mass are considered as local symptoms (S2). Systemic symptoms suggesting advanced stage disease (weight loss, fever and para-neoplastic syndromes) are defined as S3 cases [9]. Notably, asymptomatic patients have more favourable CSS rates in comparison with patients with local symptoms. Therefore, this parameter might be considered a further criterion in the decision-making process for management of T1 tumours. Haematuria is considered by some authors as a relative contraindication for PN because this sign may indicate upper collecting

system involvement. Notably, urinary collecting system (UCS) involvement is still not included in the current TNM staging system. However, Verhoest et al. in 2009 demonstrated in a large series of patients the independent role of UCS invasion to predict the cancer-specific survival of both patients with pT1 and pT2 tumours [10].

Clinical tumour size is traditionally recognized as an important prognostic factor, and it has been used as the main criterion to select patients suitable for NSS. Considering T1 tumours, international guidelines recommend NSS as standard of care for T1a tumours and strongly support expanding indications also for T1b tumours whenever technically feasible.

However, rather than size alone, it is the anatomical and topographic characteristics of T1 renal tumours as well as surgeon experience that represent the main factors influencing the technical feasibility of NSS. In 2009, two nephrometry systems, the RENAL nephrometry and PADUA classification, were proposed to classify parenchymal renal tumours according to their anatomical and topographic characteristics with the aim to predict the surgical complexity, thereby refining selection criteria for, and improving the main outcomes of, PN [11, 12]. Figure 2.1 shows the variables included in PADUA classification and the different scores applied for each anatomical situation.

Table 2.1 describes the parameters included in the RENAL and PADUA classifications. Besides a different criterion used to define longitudinal polar location (Fig. 2.2), the PADUA system includes rim location and considers involvement of urinary collecting system and of renal sinus separately (Table 2.1). In 2010, Simmons et al. described the centrality index (c-index) system, which gives a single score based entirely on tumour size and tumour depth variables. This system does not communicate data on geographic location, but provides information about the proximity of the tumour to the kidney centre [13]. Probably, the complexity to calculate this score was responsible of a more limited application of this system compared to PADUA and RENAL nephrometry scores.

Neither nephrometry systems consider the status of perirenal fat tissue as a further potential factor influencing the complexity of a PN. The presence of adherent perinephric fat is known to make tumour exposure and excision more difficult, requiring subcapsular renal dissection and hence increasing the risk of complications. In 2014, an additional scoring system, called the Mayo Adhesive Probability, has been proposed by Davidiuk et al. [14]. Based on a series of 100 patients undergoing robot-assisted PN, the authors built a scoring algorithm predicting the presence of adherent perinephric fat. The risk score was created using two image-derived variables, i.e. posterior perinephric fat thickness and stranding, which were most highly predictive at multivariable analysis. This system requires external validation on a large-scale basis before entering clinical practice. Similarly, Zheng et al. tested the role of perinephric fat density measured during preoperative CT scan to predict intraoperative fat dissection difficulty. They reported that this parameter is a strong indicator of so-called sticky fat and can anticipate more difficult PN cases [15].

Several studies demonstrated that RENAL and PADUA systems are able to predict perioperative outcomes such as ischaemia time, blood loss and intra- and post-operative complications regardless of the approach used to perform NSS [16]. Therefore, both systems are widely used in clinical practice. However, few studies compared the PADUA and RENAL systems. In 2011, Hew et al. tested the PADUA and RENAL systems in a series of 134 patients undergoing PN. Both systems predicted complications at univariable analysis. At multivariable analyses, PADUA score $\geq$ 10 (OR 3.98, p = 0.01), RENAL score $\geq$ 9 (OR 4.21, p = 0.02), tumour size (OR 1.35, p = 0.02) and age (OR 1.04, p = 0.04) were independent predictors of complications. Moreover, both scores resulted able to predict ischaemia time. Interestingly, both systems showed a substantial reproducibility with an interclass correlation coefficient of 0.73 for PADUA and 0.70 for RENAL score [16]. In 2012, Bylund et al. evaluated the association of tumour

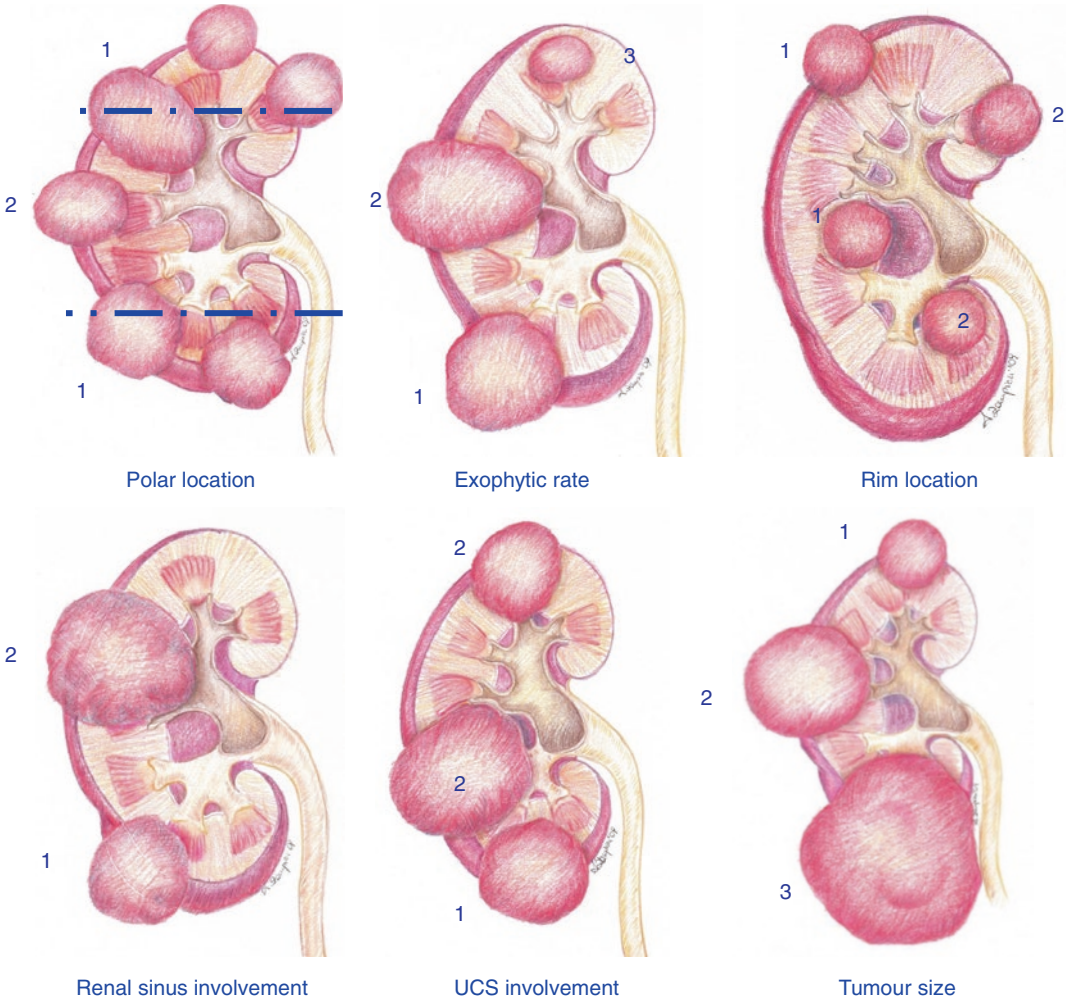

Fig. 2.1 Features included in the PADUA classification and scores applied for each anatomical situation

Table 2.1 Differences and parameters included in RENAL nephrometry and PADUA classification

Variables	RENAL	PADUA	Differences
Tumour size	≤4; 4–7; >7 cm	≤4; 4–7; >7 cm	No
Exophytic (%)	≥50%; <50%; endophytic	≥50%; <50%; endophytic	No
Polar location	Renal hilar as landmark	Sinus line as landmark	Yes
Rim location	Not evaluated	Lateral, medial	Yes
Renal sinus involvement	≤4; 4–7; >7 mm	Not involved, involved	Yes
UCS involvement		Not involved, involved	Yes
Face	Anterior/posterior	Anterior/posterior[a]	No/Yes

[a]Excluded from the score according to univariable analysis

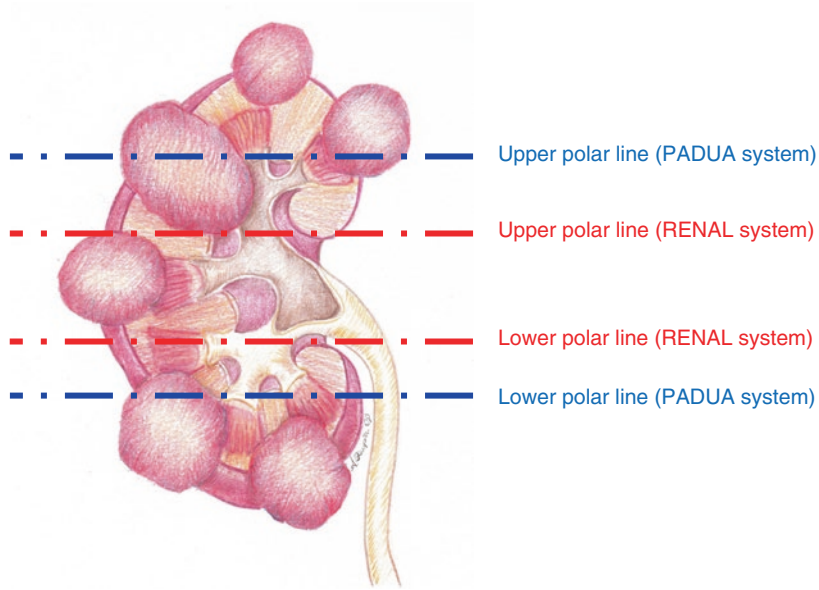

Fig. 2.2 Definition of polar lines according to PADUA and RENAL nephrometry systems

size, location, RENAL, PADUA and centrality index score with perioperative outcomes and post-operative renal function. Both PADUA and RENAL systems outperformed tumour size and location in the prediction of perioperative outcomes [17]. In 2014, Zhang et al. tested PADUA and RENAL systems in a series of 245 Chinese patients undergoing laparoscopic PN. In this retrospective study, at multivariable analysis both scores were able to predict the percent change in estimated glomerular filtration rate. Moreover, this study confirmed the reproducibility of PADUA and RENAL systems, with concordance values ranging between 0.69 and 0.89 for the various components of the PADUA and between 0.67 and 0.89 for those of the RENAL system [18].

The predictive accuracy of nephrometry systems has been demonstrated not only for PN but also for other minimally invasive treatments of renal tumours, such as cryoablation and radiofrequency ablation. Schmit et al. tested the RENAL system in a series of 751 renal tumours treated with percutaneous ablation (430 cryoablation and 321 radiofrequency ablation) [19]. The RENAL system accurately predicted treatment efficacy and complications. These systems can be applied also to the laparoscopic approach, as shown by Klatte et al. in a cryoablation series using PADUA system [20] and by Chang et al. in a radiofrequency ablation series using the RENAL system [21].

Accurate classification of the anatomical and topographic characteristics of small renal masses according to available nephrometry systems must be considered as a standard of care for the preoperative evaluation of patients suitable for NSS.

2.3 Pathological Factors

Renal tumours represent a group of entities with different cytogenetic, morphological and clinical characteristics. Moreover, approximately 20% of small renal masses are benign. In particular, papillary adenomas, pure oncocytomas and angiomyolipomas (except for a rare epithelioid variant) do not possess metastatic potential. In the context of malignant tumours, clear cell RCC represents the most common histological subtype, accounting for about 75% of all cases. The most frequent non-clear cell RCC subtypes are papillary (15%), chromophobe (5%) and Bellini duct (<1%) tumours. However, the progress in the knowledge of molecular and cytogenetic characteristics of renal cancers in the last decade has allowed pathologists to describe new subtypes, recently listed in the International Society of Urological Pathology (ISUP) Vancouver Modification of

Table 2.2 International Society of Urological Pathology (ISUP) Vancouver Modification of WHO (2004) Histologic Classification of Kidney Tumours

Renal cell tumours
Papillary adenoma
Oncocytoma
Clear cell RCC
Multilocular cystic clear cell of low malignant potential
Papillary RCC (types 1 and 2)
Chromophobe RCC
Hybrid oncocytic chromophobe tumour
Carcinoma of the collecting ducts of Bellini
Renal medullary carcinoma
MiT family translocation RCC [Xp11, t(6:11)]
Carcinoma associated with neuroblastoma
Mucinous tubular and spindle cell carcinoma
Clear cell tubulopapillary RCC
Hereditary leiomyomatosis RCC
RCC, unclassified

WHO (2004) Histologic Classification of Kidney Tumours [22] (Table 2.2).

The new renal cell tumours proposed by the ISUP in Vancouver were tubulocystic renal cell carcinoma, renal cell carcinoma associated with acquired cystic kidney disease, clear cell (tubulo) papillary renal cell carcinoma, t(6;11) translocation renal cell carcinoma with consequent re-denomination of the entire group of tumours with translocation as "MiT family translocation renal cell carcinoma" and, finally, renal cell carcinoma associated with leiomyomatosis and renal cell cancer. Of note, clear cell (tubulo)papillary renal cell carcinoma, a neoplasm originally described in the setting of end-stage kidneys and subsequently recognized in otherwise normal renal parenchyma, has been demonstrated to represent up to 4% of all renal tumours. This entity, along with tubulocystic renal cell carcinoma, renal cell carcinoma associated with acquired cystic kidney and renal cell carcinoma with t(6;11) translocation, shows an indolent behaviour in the majority of cases; none of the clear cell (tubulo)papillary renal cell carcinomas described so far has recurred. On the other hand, renal cell carcinoma associated with hereditary leiomyomatosis and renal cancer syndrome, a tumour characterized by a germline mutation in the gene coding for the enzyme fumarate hydratase, shows aggressive behaviour. Moreover, during the consensus conference, the following neoplasms were included in the group of emerging entities: thyroid-like follicular renal cell carcinoma, renal cell carcinoma associated with succinate dehydrogenase B mutation and renal cell carcinoma with ALK translocation. New concepts regarding recognized tumour entities were also proposed during the conference, including a multicystic variant of renal cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma and hybrid oncocytic tumours, collecting duct carcinoma, medullary renal cell carcinoma, mucinous and spindle cell renal cell carcinoma, angiomyolipoma as well as the epithelioid variant, cystic nephroma, mixed epithelial and stromal tumour and primary synovial sarcoma of the kidney.

While clear cell and papillary subtypes appear to stem from the epithelial cells of proximal tubule, oncocytomas and chromophobe subtypes arise from the distal tubule. Collecting duct and medullary RCCs arise from the collecting ducts of Bellini and renal medulla, respectively. Table 2.3 summarizes macroscopic, histological and cytogenetic characteristics of the main RCC subtypes [23].

Although the prognostic role of the main histological subtypes remains debated, the literature shows that papillary and chromophobe RCC have lower pathological stages and nuclear grades, as well as a lower risk of metastasis, compared to clear cell RCC. Consequently, patients with clear cell RCC have significantly lower CSS rates compared to those with either papillary or chromophobe subtypes, whereas the outcomes of papillary or chromophobe cancers are similar. Five-year CSS probabilities range from 43 to 83% for clear cell RCC, from 61 to 90% for papillary RCC and from 80 to 100% for chromophobe RCC [4]. Conversely, collecting duct and renal medullary carcinoma are commonly diagnosed at an advanced stage and have a poor prognosis after surgery. A recent multi-institutional study estimated a 5-year CSS of only 40.3% in a series of 95 patients surgically treated for Bellini tumours [24].

Table 2.3 Macroscopic, histologic and cytogenetic characteristics of main RCC subtypes

Tumour type	Gross appearance	Microscopic appearance		Cytogenetic alterations
Clear cell	Yellow, well circumscribed and can possess distinct areas of haemorrhage and necrosis	Abundant clear cytoplasm due to deposition of lipid and glycogen		3p (90%), 14q, 8p and 9p and gains at 5q and 12q
Papillary	Mixed cystic/solid consistency. Papillary RCC lesions are often reddish-brown and frequently have a well-demarcated pseudocapsule	Papillary or tubulopapillary architecture. Calcifications, necrosis and foamy macrophage infiltration	Type 1: Thin, basophilic papillae with clear cytoplasm Type 2: Heterogeneous, thicker papillae and eosinophilic cytoplasm	Gains of 7, 8q, 12q, 16p, 17 and 20 and loss of 9p. Papillary type 2 with gains of 8q, loss of 1p and 9p
Chromophobe	Large, well-circumscribed, tan-brown tumour with occasional central scar	Distinct cell borders and a voluminous cytoplasm, nuclear morphology with perinuclear halos, binucleation	Classic: Pale cytoplasm Eosinophilic: Large tumour cells with fine eosinophilic granules	Loss of chromosomes 1, 2, 6, 10, 13 and 17
Oncocytoma	Mahogany colour, well-circumscribed, occasional central scar and rarely with necrosis	Polygonal cell with abundant eosinophilic cytoplasm and uniform, round nuclei		Loss of 1p, loss of Y, often normal karyotype
Collecting duct	Partially cystic, white-grey appearance and often exhibit invasion into the renal sinus	Tubulopapillary pattern, often with cell taking columnar pattern with hobnail appearance, presence of mucinous material, desmoplastic stroma		Losses at 8p, 16p, 1p, 9p and gains at 13q
Medullary	Tan/white, poorly defined capsule, extensive haemorrhage and necrosis	Poorly differentiated, eosinophilic cell; inflammatory infiltrative cells; sheet-like or reticular pattern common		Poorly described, but believed normal karyotype
MiT family	Yellowish tissue often studded by haemorrhage and necrosis	Papillary or nested architecture, granular and eosinophilic cell with voluminous, cytoplasm		Recurrent translocations involving Xp11.2 (TFE3) or 6p21 (TFEB)

Besides tumour characterization according to histological subtype, the most important traditional pathological factors dictating the prognosis of patients with RCCs are the pathological size and extent of the primary tumour, nuclear grading, coagulative necrosis, microvascular invasion and sarcomatoid dedifferentiation.

pT1 tumours based on the latest TNM staging system represent more than 60% of cases included in the largest cohort studies. Specifically, pT1a tumours account for about 35% of cases and pT1b for 27% of cases. The estimated 5-year CSS was approximatively 95% in pT1a tumours and 93% in pT1b. Interestingly, 5-year CSS rates of pT1 tumours were significantly higher compared to pT2a tumours (estimated around 70%) [25]. Moreover, literature data confirm that in pT1 tumours the oncologic outcomes are equivalent after PN and RN [26, 27]. However, when critically examining these data, one has to note that in the subgroup of T1b tumours treated with PN mean tumour size ranged from 5 to 5.5 cm. Interestingly, a multi-institutional study in 2005 showed that 5.5 cm was the most accurate cut-off size to stratify organ-confined RCC in

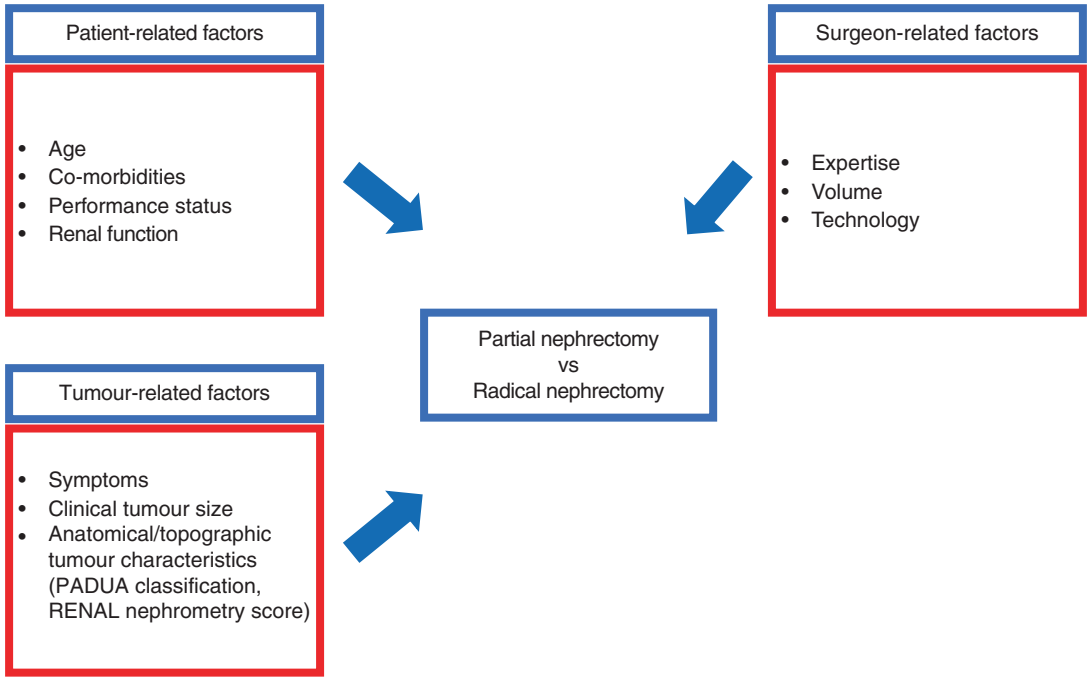

Fig. 2.3 Factors influencing the decision-making for partial or radical nephrectomy

two different categories according to CSS probabilities [28]. These data should be considered at the time of preoperative counselling of patients with cT1b tumours larger than 5 cm and suitable for NSS.

The four-tiered Fuhrman grade classification has been the most frequently used system in the last decades. Interestingly, looking at pT1 tumours, some authors reported a direct correlation between tumour size and nuclear grading. Indeed, Ficarra et al. showed that mean tumour size was 4 cm for grade 1, 5.5 cm for grade 2, 7 cm for grade 3 and 9 cm for grade 4, respectively. Therefore, pT1a tumours have more frequently grade 1 or grade 2. Conversely, grade 3 or grade 4 tumours are more frequent in the pT1b or pT2 cases [29]. Interestingly, several studies confirmed the independent role of the Fuhrman nuclear grading to predict CSS and progression-free survival in patients with clear cell RCC. Conversely, the prognostic role of nuclear grade is controversial for papillary or chromophobe RCC [4]. With all these limitations, results of large multi-institutional studies showed that 5-year survival probabilities were 86–89% for grade 1 tumours, 72–79% for grade 2 tumours, 50–60% for grade 3 tumours and 28–30% for grade 4 tumours [4].

Similarly, the prognostic role of coagulative necrosis has uniformly been shown in several retrospective studies including clear cell RCC, but it is still controversial in other histological subtypes [4]. Clearly, the presence of coagulative necrosis is more common in patients with larger tumours. Data from the Mayo Clinic showed that tumour necrosis was present in less than 30% of clear cell RCC, in around 45% of papillary RCC and in 20% of chromophobe RCCs. The risk ratio for death from RCC in patients with necrotic compared with non-necrotic tumours was 5.27 for clear cell, 4.20 for chromophobe and 1.49 (absent) for papillary RCC [30]. Figure 2.3 shows the factors influencing the choice of surgical treatment.

2.4 Predictive Mathematical Models

Several mathematical models have been developed to estimate the risk of disease recurrence or progression as well as of CSS and OS in patients with RCC. Some of these models are based on preoperative clinical factors only, others combine clinical and pathological variables and others consider pathological variables only [8]. Notably, none of these predictive tools have been specifically designed for patients with localized renal tumours suitable for PN.

Age, gender, presence of symptoms, clinical tumour size and clinical stage according to TNM classification are the most relevant preoperative variables combined in the context of the most important preoperative mathematical models. Race was only included in the Kutikov nomogram [31]. Most of these tools have been tested to predict recurrence-free survival, CSS and/or OS after PN or radical nephrectomy.

Table 2.4 summarizes the characteristics and the accuracy rates of the most common preoperative tools proposed to predict the prognosis of patients suitable for PN or radical nephrectomy [31–34]. The Karakiewicz nomogram seems to be the best tool to predict CSS in patients suitable for radical nephrectomy or PN.

Histological tumour subtypes, pathological tumour size and TNM staging, nuclear grading and coagulative necrosis are the pathological variables most frequently included in the mixed or pure pathological models predicting RFS, CSS or OS [35]. Table 2.5 summarizes the clinical and pathological parameters included in each model and reports the accuracy rates of most common integrated models including pathological information [36–40]. Figure 2.4 summarizes the key prognostic factors of patients with renal cell carcinoma.

Table 2.4 Characteristics and accuracy of the most important preoperative tools proposed to predict the prognosis of patients suitable for partial or radical nephrectomy

Authors	Variables	Treatment	Outcomes	Accuracy
Yaycioglu, 2001 [32]	– Symptoms – Clinical size	Radical and partial nephrectomy	RFS CSS OS	0.65 0.62 0.58
Cindolo, 2003 [33]	– Symptoms – Clinical size	Radical and partial nephrectomy	RFS CSS OS	0.67 0.64 0.61
Karakiewicz, 2009 [34]	– Age – Gender – Symptoms – Clinical size – cT – M	Radical and partial nephrectomy	CSS	0.84–0.88
Kutikov, 2009 [31]	– Race – Age – Gender – Clinical size	Radical and partial nephrectomy	CSS OS	0.70–0.73

Table 2.5 Accuracy of most common integrated models including histopathological information

Authors	Histologic subtypes	Variables	Outcomes	Accuracy [33]
Kattan, 2001 [36]	All	– Symptoms – Hystotype – pSize – pT (1997)	RFS CSS OS	0.80 0.77 0.70
Zisman, 2001 [37]	All	– Performance status – pTNM – grading	CSS OS	0.79–0.84 0.64–0.86
Frank, 2002 [38]	Clear cell RCC	– pSize – pT – pN – M – Necrosis – grading	RFS CSS	0.82 0.83–0.88
Sorbellini, 2005 [39]	Clear cell RCC	– Symptoms – pSize – pT (2002) – Grading – Necrosis – Vascular invasion	RFS	0.82
Karakiewicz, 2007 [40]	All	– Symptoms – pSize – pT (2002) – pN – M – Grading	CSS	0.86

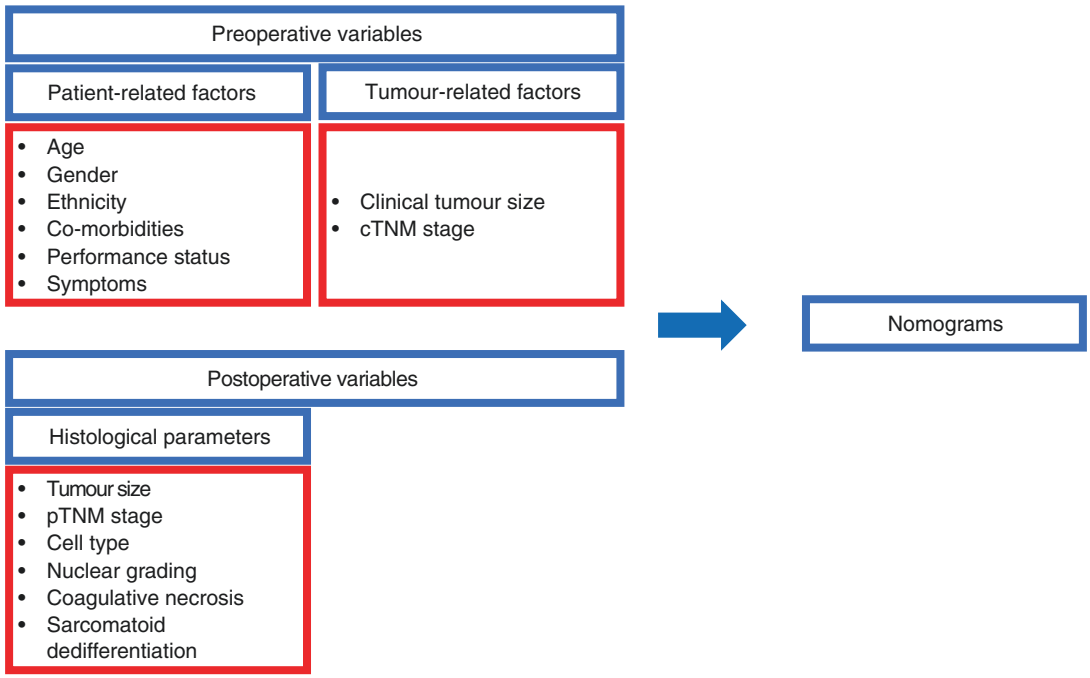

Fig. 2.4 Clinical and pathological factors influencing the prognosis of patients with renal cell carcinoma

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Diagnostic Modalities

3

Elstob Alison, Uday Patel, and Michael Gonsalves

Abbreviations

CT	Computed tomography
CECT	Contrast-enhanced CT
CEUS	Contrast-enhanced ultrasound
DWI	Diffusion-weighted imaging
FSE	Fast spin echo
FDG	Fluorine-18 fluoro-2-deoxyglucose
GRE	Gradient-recalled echo
PET	Positron emission tomography
RCC	Renal cell carcinomas
US	Ultrasound

Key Messages

- Incidental detection of small renal masses is increasingly common, and these masses require accurate characterisation with imaging to facilitate management decisions.
- Contrast-enhanced CT (CECT) has high diagnostic accuracy for the diagnosis of RCC and remains the mainstay for radiological evaluation of both cystic and solid lesions.
- MRI and contrast-enhanced US are good techniques for problem-solving in lesions deemed indeterminate by CECT or for patients in which CECT is contraindicated.
- In a mass that demonstrates measurable enhancement on CT or MRI, no specific imaging features can conclusively distinguish between RCC and oncocytoma.
- Percutaneous biopsy should be considered in lesions that remain indeterminate after initial imaging investigations.

3.1 Background

Over the last decade, the incidence of renal cancer in the United Kingdom has increased by almost a third [1]. This is largely attributable to

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increased incidental detection, due to the widespread use of cross-sectional imaging. Currently, between 50 and 61% of all renal cancers are detected incidentally, compared with only 13% in the 1970s [2, 3]. There has been an associated stage migration with incidentally detected renal cell carcinomas (RCC) tending to be of both lower stage and grade. Optimum management of small renal tumours poses a particular challenge to the renal cancer multidisciplinary team, for two key reasons. Firstly, up to 20% of renal masses smaller than 4 cm in diameter are benign [4–6]. Secondly, there are multiple management strategies available to clinicians including nephrectomy, partial nephrectomy, ablation and observation. Accurate characterisation of renal masses is therefore fundamental to achieving the best outcomes for patient with small renal tumours. In this chapter, the different imaging modalities will be evaluated, and their role in characterising both small cystic and solid renal lesions will be discussed.

The Goals of Imaging: Key Questions to Be Answered

1. Is the mass solid or cystic?
2. Is the mass benign or malignant?
3. Does the tumour exhibit features of biological aggressiveness?
4. What anatomical information can be provided to aid surgical treatment and decision-making?

3.2 Computed Tomography

CT is the primary imaging modality used for identification and characterisation of small renal masses. In this section we will discuss the imaging features that enable differentiation between solid and cystic lesions and potentially between benign and malignant lesions. While these features are discussed in the context of CT imaging, they are applicable to other imaging modalities.

Accurate CT evaluation of a small renal mass can only be achieved with reference to the clinical history of the patient. The majority of inflammatory, vascular or post-traumatic "pseudotumours" can be diagnosed correctly when the clinical history highlights the possibility of these conditions (Fig. 3.1).

3.2.1 Enhancement

Enhancement of renal masses is considered to be the most important factor in distinguishing between a cyst and a solid renal mass [7, 8]. A renal mass protocol CT must therefore include images obtained before and after administration of iodinated contrast media. Post-contrast images should be obtained during the nephrographic phase (85–120 s post-contrast administration) as there is maximal and homogeneous enhancement of renal parenchymal, increasing the conspicuity

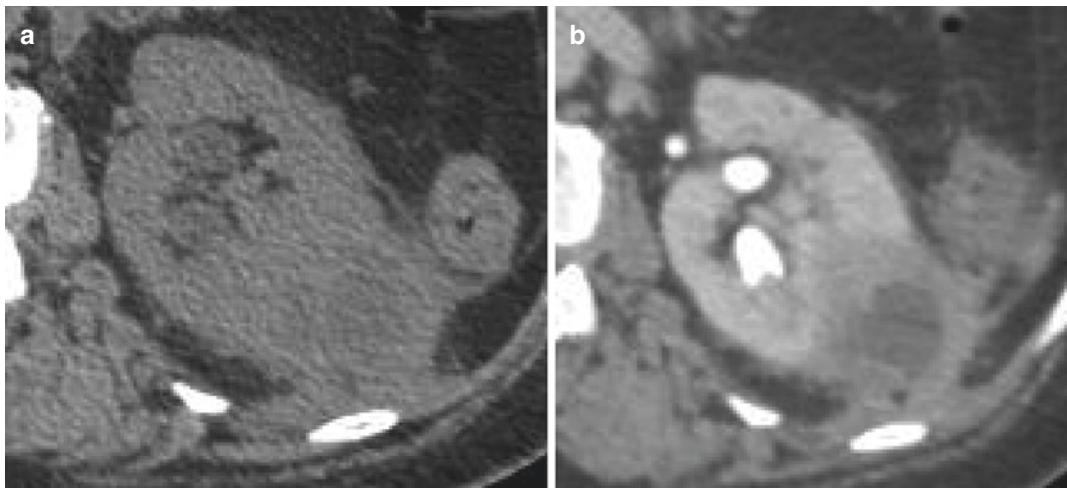

Fig. 3.1 Pre- (**a**) and (**b**) post-contrast axial CT images demonstrate a rim enhancing left interpolar lesion with adjacent perinephric stranding. Aspirated material cultured *E. coli*

of renal masses. An increase in the attenuation of a renal lesion of at least 20 Hounsfield units (HU), following contrast administration, represents definitive enhancement and is in keeping with a solid lesion or solid component [8]. A lesion with post-contrast enhancement of less than 10 HU is classed as non-enhancing. Lesions enhancing by 10–20 HU are considered to be indeterminate and will require further characterisation (Figs. 3.2, 3.3, 3.4 and 3.5).

The main limitation of the use of enhancement is lesion size. As lesion size decreases, sampling error and image artefacts can lead to erroneous attenuation measurements and potential misclassification of renal lesions [8, 9]. Multiple authors have questioned the reliability of attenuation measurements in sub-centimetre masses.

3.2.2 Macroscopic Fat

Macroscopic fat within a solid renal lesion is highly suggestive of angiomyolipoma (AML), the commonest benign renal neoplasm. Macroscopic

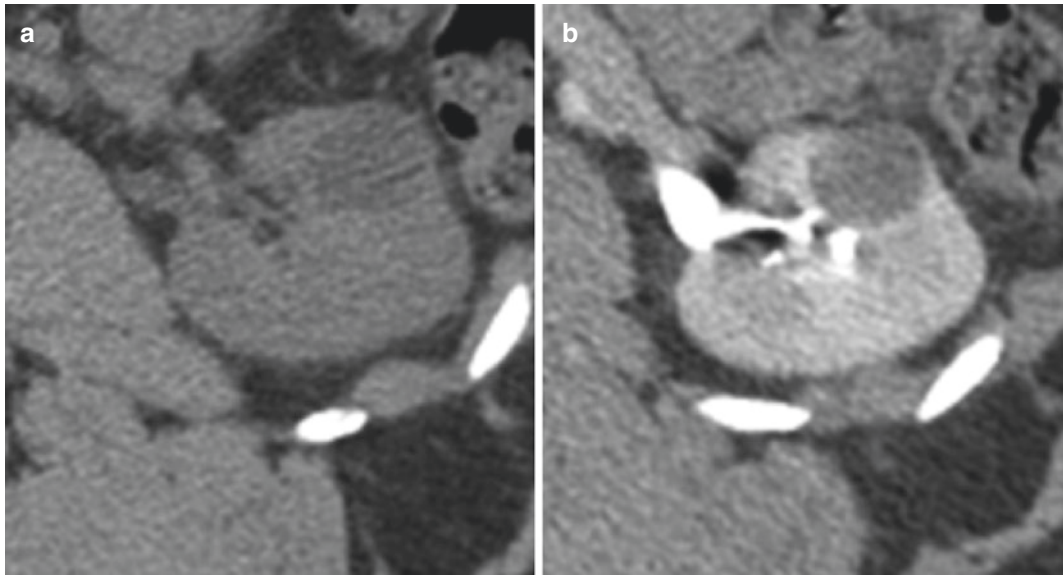

Fig. 3.2 Simple cyst. Pre- (**a**) and (**b**) post-contrast axial CT images demonstrate enhancement of less than 10 HU

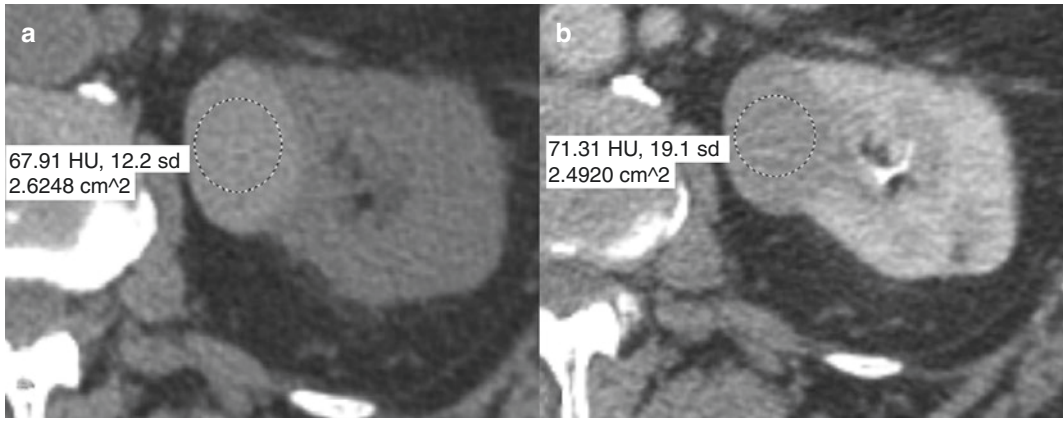

Fig. 3.3 Pre- (**a**) and (**b**) post-contrast axial CT images demonstrate indeterminate enhancement of 14 HU. This was confirmed as a hyperdense cyst on ultrasound

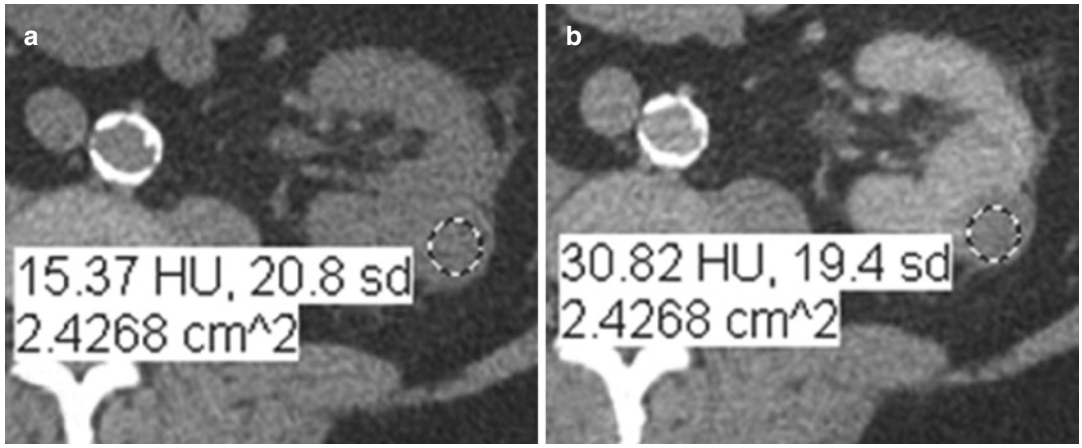

Fig. 3.4 Pre- (**a**) and (**b**) post-contrast axial CT images demonstrate indeterminate enhancement of 15 HUs. Histology confirmed a papillary type 1 RCC

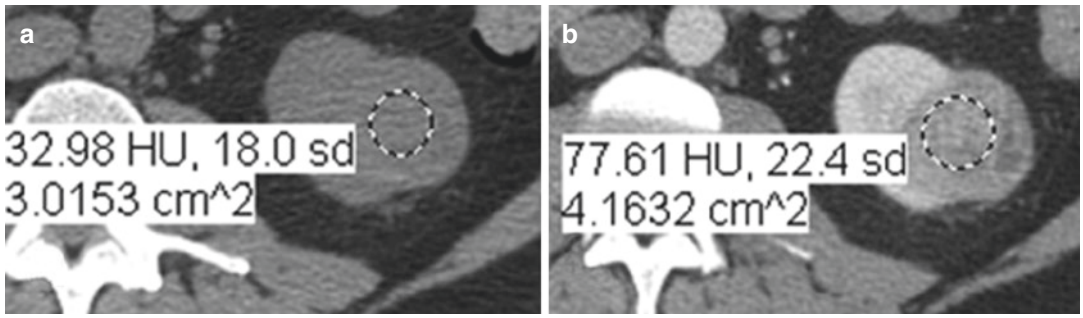

Fig. 3.5 Pre- (**a**) and (**b**) post-contrast axial CT images demonstrate post-contrast enhancement of 45 HU. Histology confirmed a clear cell RCC

fat is best demonstrated on unenhanced CT, where it returns characteristic low attenuation, measuring between −10 HU and −100 HU (Fig. 3.6).

AMLs are pathologically classified as choristomas, containing muscle, fat and vascular tissue. The relative proportions of these tissues vary between AMLs, but the majority of lesions are fat-rich, resulting in the classical imaging finding of macroscopic fat. 3–4.5% of AMLs contain microscopic fat not detectable by CT [10, 11] and can be misdiagnosed as RCC. Further diagnostic confusion can arise in the setting of RCCs containing macroscopic fat [12–15]. Various mechanisms have been described to explain the presence of intra-tumoural fat including engulfment of perinephric or renal sinus fat [14], osseous metaplasia [12] and cholesterol necrosis [15]. A potential differentiator between fat-poor AML and fat-containing RCC is the presence of coexisting calcification [12], which occurs within fat-containing RCC but is extremely rare in AML (Figs. 3.7 and 3.8).

3.2.3 Growth Rate

Multiple studies have demonstrated growth rate to be of limited utility in distinguishing between benign and malignant renal masses. Small renal tumours grow slowly regardless of histopathological subtype with average growth rates reported to be 0.28 cm/year (range of 0.09–0.86 cm/year) [16]. 70% of small renal masses under imaging

surveillance will not exhibit measurable growth during follow-up periods of up to 32 months [17–20], and Kunkle et al. found that enhancing renal lesions that did not grow during a 24-month follow-up period were about as likely to be malignant (83%) as the lesions that did exhibit growth (89%) [20]. Several authors have reported no statistically significant difference in growth rates between small RCCs and oncocytomas [16, 21].

Fast growth rates during early follow-up within the first year are a potentially useful indicator of aggressive tumours. In a meta-analysis of 284 solid lesions, only 2% of patients developed metastases at a mean follow-up of 33.5 months. However, the mean growth rate of the metastatic group was double that of other lesions, at 0.8 cm/year [22] (Figs. 3.9 and 3.10).

Fig. 3.6 Coronal post-contrast CT image demonstrates a right upper pole lesion containing macroscopic fat

3.2.4 Central Scar

Oncocytomas are the second commonest benign renal neoplasm, accounting for approximately 3–7% of all renal lesions [23]. The presence of a central stellate scar is often suggested as a feature of oncocytoma; however, this is not a reliable imaging finding. Less than half of all oncocytomas show a central scar [24] with some authors reporting this feature to be present in as few as 11% of cases [25]. Necrosis within RCC can lead to central areas of low attenuation mimicking a scar. There is currently no CT imaging feature that reliably distinguishes RCC from oncocytoma (Figs. 3.11 and 3.12).

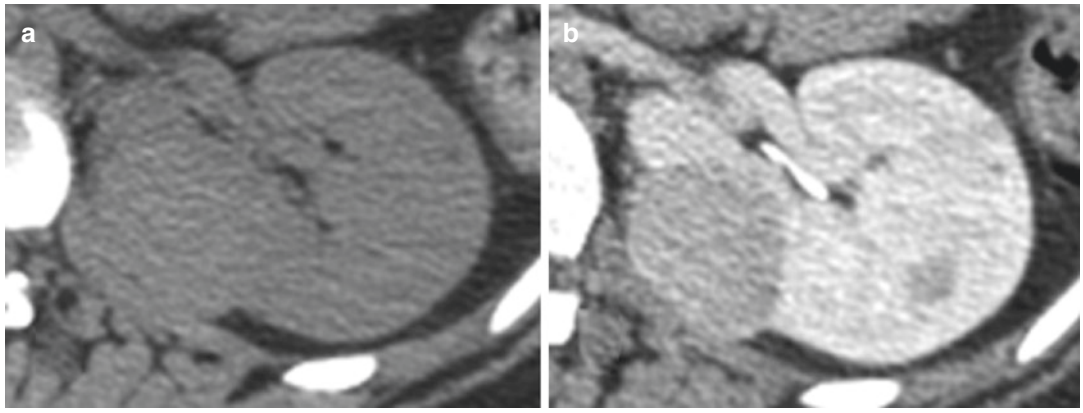

Fig. 3.7 Pre- (**a**) and (**b**) post-contrast axial CT images demonstrate an enhancing lesion with no visible macroscopic fat in a patient with tuberous sclerosis. Biopsy proven as an AML

3.3 CT of Small Cystic Renal Masses

Renal cysts are common, estimated to be present in 50% of adults over 50 years of age [26]. However, as 6% of asymptomatic renal masses have been shown to be cystic renal malignancies [27], a robust method for evaluating cystic renal masses is required. The Bosniak classification of renal cystic lesions was first described in 1986 and has subsequently gained widespread acceptance [8, 28]. Bosniak described five categories of cystic renal mass ordered in increasing probability of malignancy (summarised in Table 3.1 and Fig. 3.4).

Fig. 3.8 Post-contrast axial CT image demonstrates an enhancing mass containing macroscopic fat and a small focus of peripheral calcification. Biopsy proven as a papillary RCC type 1

A series evaluating 116 cystic renal masses found good concordance between Bosniak classification and histopathology, with the authors concluding that Bosniak classification is useful for separating surgical from non-surgical cystic lesions [29]. High-quality CT is critically important in the accurate characterisation of cystic renal masses [29–31] (Fig. 3.13).

3.4 Morphometric Scoring Systems

In the last 5 years, several systems have been proposed to help evaluate the anatomical complexity of small renal masses. The main catalyst for these scoring systems has been shift in surgical practice towards treating a greater proportion of small renal masses with partial rather than radical nephrectomy. The R.E.N.A.L. nephrometry score and PADUA classification systems are the most widely used and are clearly outlined in their original articles [32, 33].

Other scoring systems have been described including the C index method that evaluates the single anatomical feature of proximity of tumour to the central renal sinus [34], renal tumour inva-

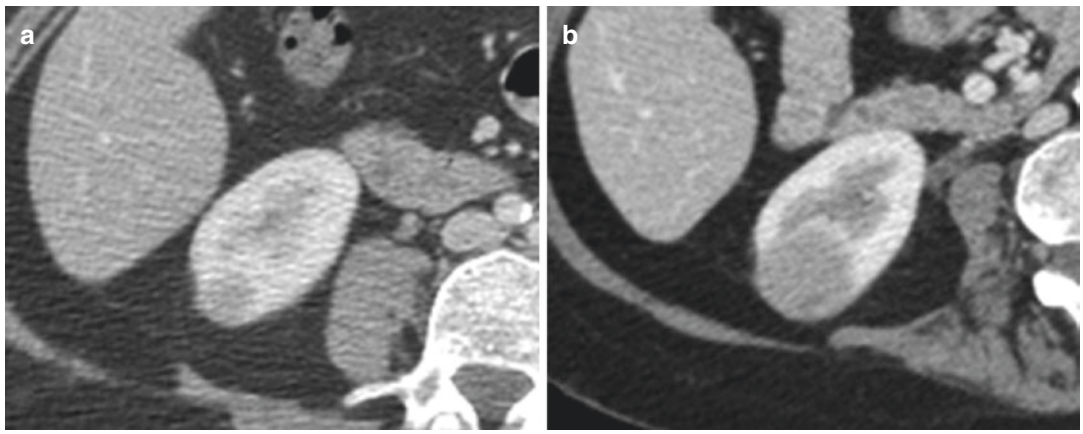

Fig. 3.9 (**a**, **b**) Post-contrast axial CT images of a clear cell RCC over a 5-year period showing typical slow growth

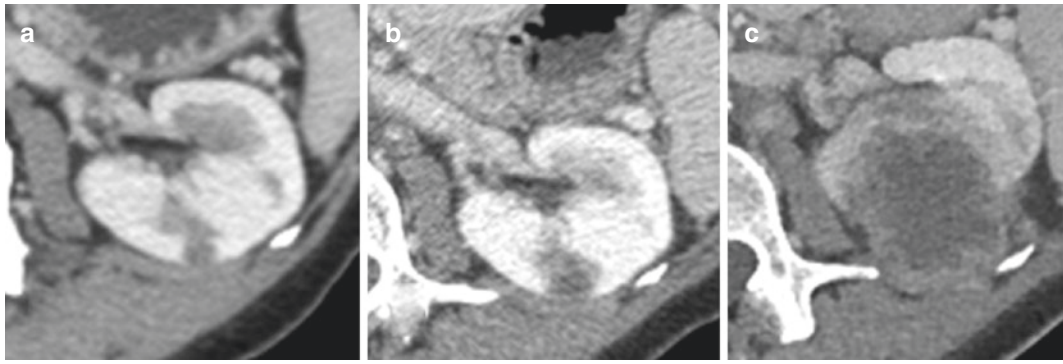

Fig. 3.10 Serial post-contrast axial CT images of renal mass in a patient with lung cancer, at baseline (**a**), at 3 months (**b**) and at 6 months (**c**). The mass demonstrated rapid growth. Biopsy proven as metastasis from the primary SCC of the lung

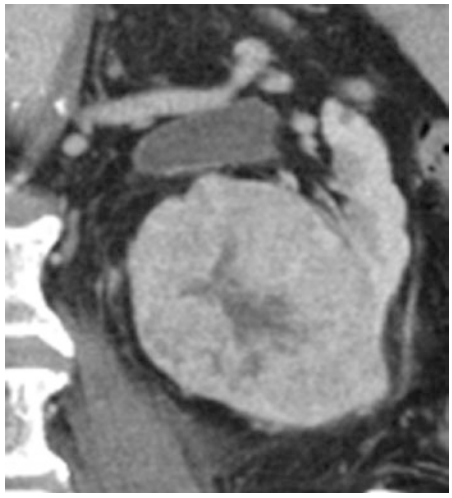

Fig. 3.11 Coronal post-contrast CT image of a left lower pole lesion with central scar. Histology confirmed this to be an oncocytoma

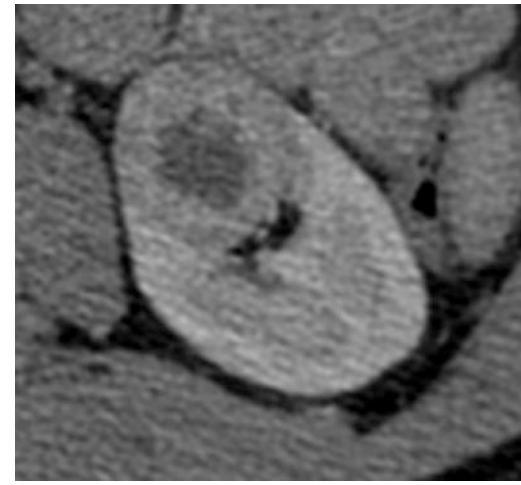

Fig. 3.12 Axial post-contrast CT image of an enhancing left renal mass with a central area of low attenuation which mimicked a scar. Histology proven to be a clear cell RCC

Table 3.1 Bosniak classification of renal cystic lesions (adapted from reference 8, Israel and Bosniak 2005)

Category	Imaging features	Management
I	Water attenuation, hairline thin wall with no septa, calcifications or solid components. No enhancement	No intervention Benign, simple
II	Few hairline thin septa that may enhance (not measurably). Fine calcification or short segment of thickened calcification in wall or septa Or uniformly high-attenuation lesion <3 cm that does not enhance	No intervention Benign
IIF	Multiple hairline thin septa, perceived (not measurable) enhancement of septa or wall Minimal thickening of septa or wall. Thick or nodular calcification in wall or septa Totally intrarenal, non-enhancing high-attenuation lesions >3 cm	Requires follow-up
III	Thickened smooth or irregular walls and/or septa in which measurable enhancement is present	50% malignant Intervention required as neoplasm cannot be excluded
IV	Distinct enhancing soft tissue components independent of the wall or septa. Also have features of category III lesions	Resection Clearly malignant

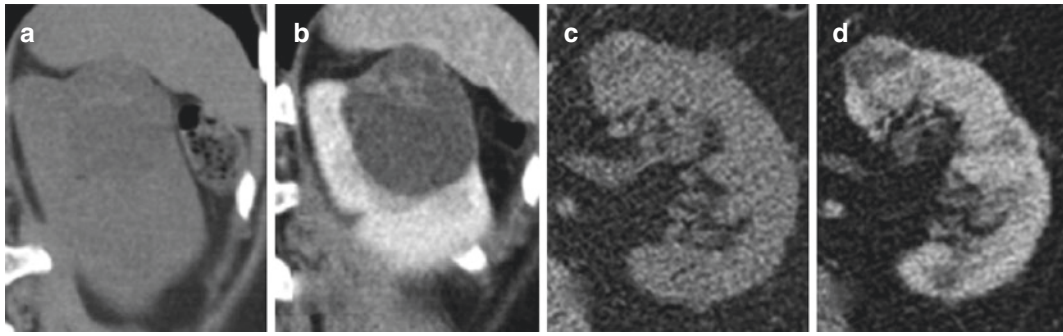

Fig. 3.13 Pre- (**a**) and (**b**) post-contrast coronal images of a left upper pole lesion with enhancing, irregular septa consistent with a Bosniak III lesion. Pre- (**c**) and (**d**) post-contrast axial images of a Bosniak IV cystic left renal lesion containing an enhancing soft tissue nodule

sion index that quantifies tumour depth invasion into renal parenchyma [35] and renal pelvic score that assesses renal pelvis anatomy irrespective of renal tumour features [36].

Research has already begun evaluating these scoring systems to help risk-stratify patients undergoing partial nephrectomy (PN) and investigating whether these scores can predict surgical and oncological outcomes. Studies have shown that patients with higher scores have increased intraoperative complications [37, 38] and post-operative complications [39]. However, these studies have included predominately open PN and some laparoscopic PN series with more varied outcomes reported following robotic-assisted PN [40]. Higher morphometric scores have also been associated with increased risk of metastases and death from RCC, but further studies are needed to validate these relationships [41].

CT is the imaging workhorse in the evaluation of small renal masses. However, there are situations when MRI or ultrasound should be considered. Patients who cannot receive iodinated contrast media due to allergy or advanced kidney disease and individuals with genetic predisposition to renal tumours, who are likely to undergo serial imaging, should be offered alternate imaging modalities.

3.5 Magnetic Resonance Imaging (MRI)

MRI offers a reliable alternative to CT for the evaluation of small renal masses and is the imaging modality of choice in patients who are allergic to iodinated contrast media. While MR contrast agents cannot be administered safely in end-stage renal failure, an unenhanced MRI is likely to yield better diagnostic information than unenhanced CT. MRI is also useful in patients who are likely to undergo serial imaging, to diminish the burden of ionizing radiation.

3.5.1 Protocol

MRI protocols used to evaluate renal masses vary depending on the manufacturer and institution. However, a generic renal mass protocol should include T2 fast spin echo (FSE) in three planes, axial T1 in and out of phase, fat-saturated 3D gradient-recalled echo (GRE) pre- and post-contrast (gadolinium) and diffusion-weighted imaging (DWI).

3.5.2 Enhancement

As with CT, the presence of enhancement following intravenous contrast is a key factor in distinguishing solid renal neoplasms from cysts. However, unlike CT, the tissue dose response to MRI contrast agents is non-linear, and consequently there is no universally accepted technique for measuring enhancement [8]. Described techniques include subjective, visual comparison [8, 42], image subtraction [8, 42–44] and quantitative increase in signal intensity [42, 44].

A quantitative increase in the signal intensity returned from a renal mass on post-gadolinium

T1-weighted images, of greater than 15%, is considered to represent enhancement. This 15% threshold for signal intensity increase will yield a 100% sensitivity for renal tumour and result in a lower than 6% false positive rate [46]. Subtraction imaging involves digital subtracting unenhanced T1-weighted images from an identical sequence performed post-contrast administration. This technique has a reported 99% sensitivity for solid renal tumours [44]. There is evidence the superior contrast resolution of MRI may overcome the problem of CT pseudoenhancement, allowing more accurate characterisation of small renal masses [8, 42] (Fig. 3.14).

3.5.3 Soft Tissue Characterisation

MRI provides superior soft tissue contrast compared with CT, which confers a number of potential advantages when evaluating small renal masses.

Macroscopic fat, indicating AML, can be readily identified within small renal masses on conventional T1, T2 and fat-suppressed sequences. There is evidence to suggest MRI may have utility in differentiating fat-poor AMLs from fat-containing RCCs based on the T2 signal characteristics of these lesions. Fat-poor AMLs are hypointense on T2-weighted images due to the smooth muscle content, whereas clear cell RCCs are hyperintense [11, 47]**.** However, the diagnosis of fat-poor AMLs cannot be confidently based on this feature alone, as papillary RCCs can also demonstrate hypointensity on T2-weighted sequences [48] (Fig. 3.15).

Standard MRI sequences have not been shown to offer any greater sensitivity than CT in distinguishing between RCC and oncocytoma. Beer et al. found that both MRI and CT classified all oncocytomas within their series as surgical lesions [49]. Hecht et al. also classified all oncocytomas evaluated with MRI as malignant lesions [44]. This reflects a long-standing challenge in renal imaging, where no definite imaging features have been identified to distinguish oncocytoma from RCC. More recently, DWI has shown promise in the differentiation of RCC from oncocytoma, with one large meta-analysis demonstrating a statistically significant difference between the diffusion characteristics of these lesions [50].

The superior soft tissue contrast of MRI affords better visualisation of cyst contents and septations. In calcified cystic lesions, enhancement

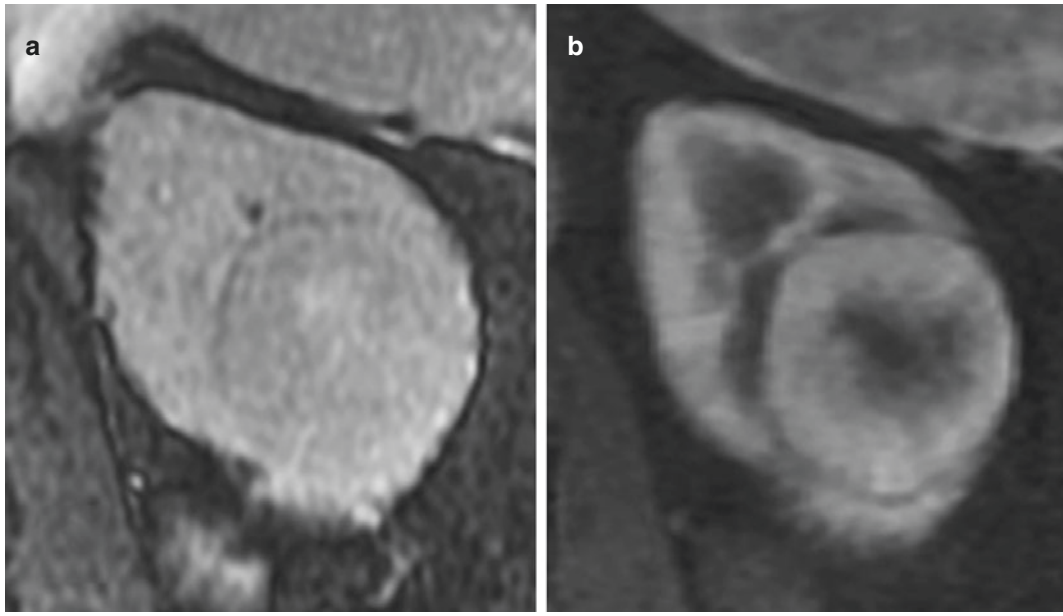

Fig. 3.14 Coronal T1-weighted (**a**) and post-contrast T1-weighted (**b**) images of a left lower pole renal mass demonstrating enhancement. Histology confirmed an RCC

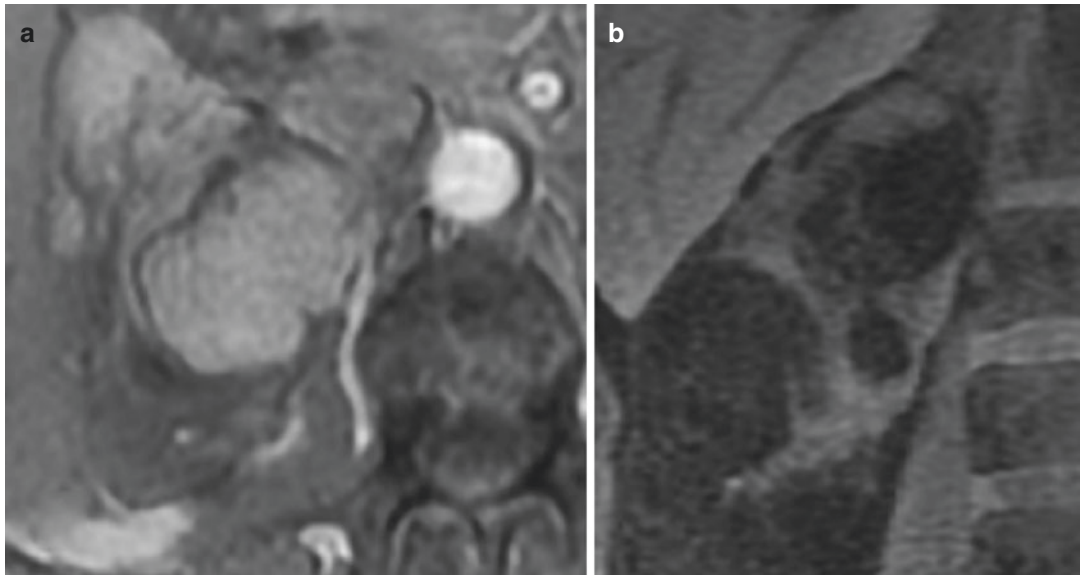

Fig. 3.15 Axial T1-weighted (**a**) and coronal fat-suppressed (**b**) sequences of an AML demonstrate macroscopic fat within the lesion

may also be better evaluated by MRI as, unlike CT, calcifications do not mask enhancement. In one study comparing MRI and CT evaluation of Bosniak cysts, MRI tended to upgrade the Bosniak category due to depiction of additional septa, improved visualisation of the cyst wall, septal thickening and enhancement. However, in this cohort of 69 renal masses, only two lesions were upgraded from non-surgical to surgical [7]. Beer et al. reported that of 56 lesions, none were upgraded from non-surgical to surgical lesions by MRI [49] (Fig. 3.16).

3.6 Ultrasound

Greyscale US is useful in distinguishing between solid and cystic renal masses; however, traditionally it has not played a further role in the evaluation of solid renal masses. With the advent of microbubble contrast agents, contrast-enhanced ultrasound (CEUS) has shown potential in the further evaluation of renal lesions. Microbubbles demonstrate tissue perfusion characteristics that are analogous to post-contrast enhancement seen with CT and MRI. Due to their size, microbubbles remain entirely intravascular which makes CEUS exquisitely sensitive to blood flow and can demonstrate minimal flow not visible by CT. CEUS is increasingly utilised as a problem-solving tool in masses when enhancement is inadequately characterised by cross-sectional imaging. Microbubbles have an excellent safety profile [51] and can be used in patients with impaired renal function. The European Federation of Societies for Ultrasound in Medicine currently recommends CEUS for the characterisation of solid renal masses [52] (Fig. 3.17).

CEUS has also been used to evaluate solid renal lesions with encouraging results. Several small studies have examined the enhancement patterns of solid renal neoplasms, in particular comparing RCC and AMLs. Certain features including heterogeneous enhancement, enhanced peritumoural rim enhancement and early washout have been strongly associated with RCC [53–55].

CEUS is also proving of value in the assessment of cystic renal lesions. Several authors have compared CEUS with CT in the evaluation of cystic renal masses. Ascenti et al. found high concordance between CEUS and CECT in the characterisation of cystic lesions and 100% concordance between the modalities in categorising lesions as surgical or non-surgical [56]. Other studies support this, reporting CEUS to have a comparable diagnostic accuracy to CECT [57–59].

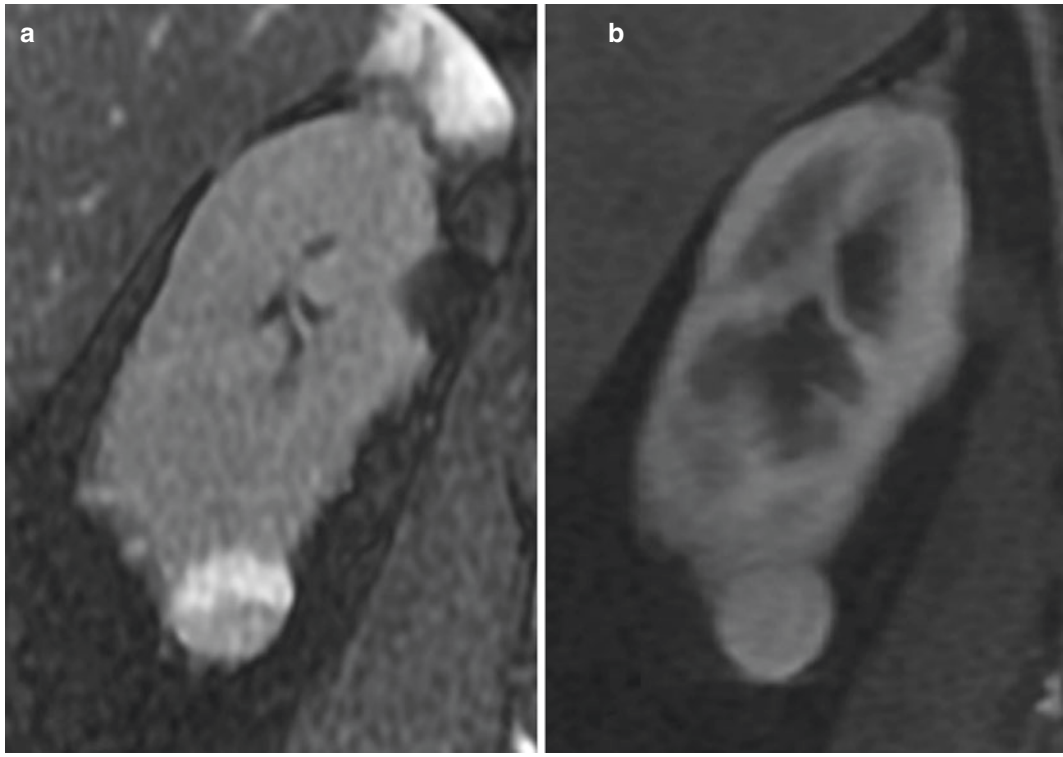

Fig. 3.16 Coronal T1-weighted MRI sequences pre- (**a**) and post-contrast (**b**) demonstrate no enhancement of the exophytic right lower pole lesion, consistent with a hyperdense cyst

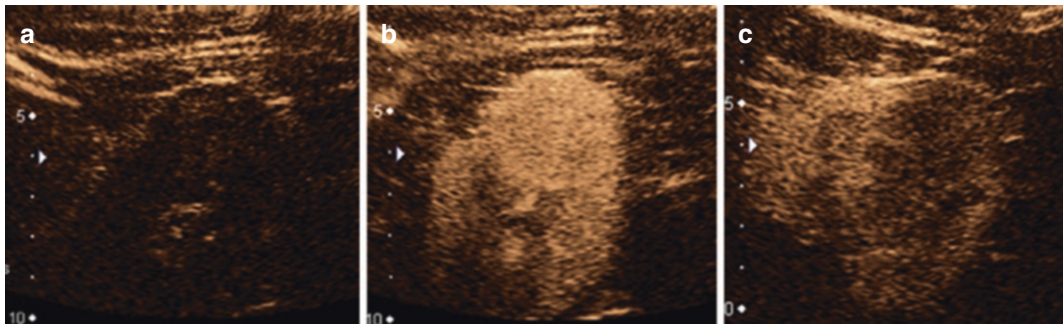

Fig. 3.17 CEUS showing typical enhancement pattern of a RCC. Figure (**a**) pre-contrast, with prompt enhancement in the early phase (**b**), and early washout (**c**). This lesion demonstrated indeterminate enhancement on preceding CT. Histology confirmed a papillary RCC

3.7 Positron Emission Tomography

Fluorine-18 fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) relies upon the cellular uptake of glucose to accumulate radiotracer within lesions in order to characterise them. Currently the role of FDG PET in small renal masses is limited for two key reasons. Firstly, normal renal parenchyma has high activity on FDG PET imaging tending to obscure small renal masses, and secondly FDG uptake is highly variable in RCC. Several studies have con-

firmed that PET has a more variable and overall poorer diagnostic accuracy in detecting RCC than CT [60–63]. Novel radiotracers may provide unique ways to characterise renal masses [64, 65], but these remain as research tools and have yet to find routine clinical application (Fig. 3.18).

3.8 Imaging-Guided Percutaneous Biopsy

Percutaneous biopsy of renal masses had largely fallen out of favour prior to the turn of the century, as the diagnostic accuracy of this procedure did not significantly outperform that of cross-sectional imaging. In a series of 2474 biopsies reported by Lane et al., percutaneous biopsy only achieved a sensitivity and specificity of 70% and 60%, respectively, for the diagnosis of RCC [66]. With advances in imaging-guided percutaneous biopsy techniques and simultaneous developments in histological analysis, this technique now has an increasing role in the characterisation of small renal masses.

The benefits of obtaining a histological diagnosis are clear and include identifying surgical lesions from those found to be indeterminate on imaging, obtaining specific tumour subtype and grade information to help prognostication and guide systemic treatment and obtaining histological confirmation of malignancy prior to commencing ablative treatments such as radiofrequency ablation and cryotherapy.

Current imaging-guided biopsy techniques have sensitivities of 70–100% and specificity of 100% [66–74]. Small lesion size has been shown to negatively affect the diagnostic performance of percutaneous biopsy. Rybicki et al. reported lesions of 4–6 cm having greatest sensitivity and NPV of 97% and 89%, respectively, in comparison to 85% and 60% for lesions smaller than 3 cm [73]. Percutaneous biopsy has been shown to have a good safety profile with low rates of complications. Tumour seeding is only rarely encountered with only seven cases reported in the literature [75] (Fig. 3.19).

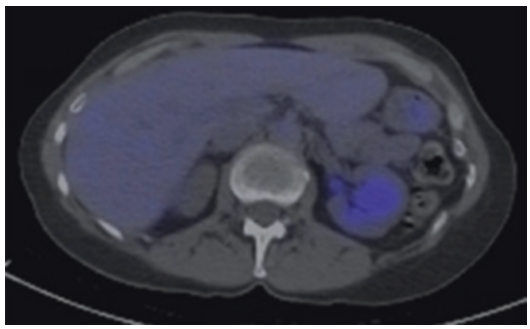

Fig. 3.18 Axial fused FDG PET-CT image demonstrating low-grade FDG avidity in the left kidney

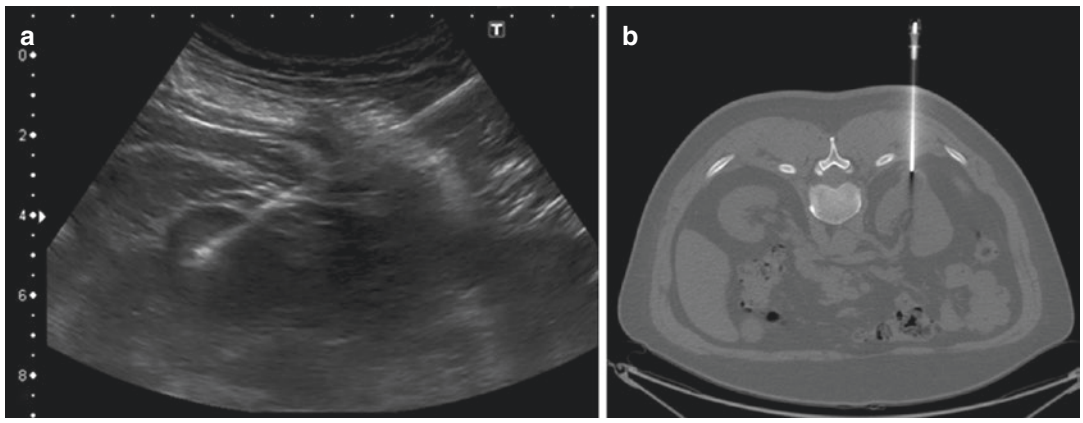

Fig. 3.19 Ultrasound-guided (**a**) and CT-guided (**b**) biopsy of a renal mass

Conclusions

Incidental detection of small renal masses on imaging, undertaken to evaluate unrelated symptoms or conditions, is a common occurrence. Subsequent management of small renal masses is dependent upon accurate imaging characterisation. Most small renal masses can be classified into surgical or non-surgical lesions by CT. However, in cases which are indeterminate by CT criteria, further investigation with MRI or CEUS will often lead to a definitive diagnosis. Considering the central role that imaging plays in the management of small renal masses, all clinicians involved in renal cancer treatment should have an understanding of the interpretation and diagnostic performance of the relevant imaging modalities.

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The Role of Renal Biopsy

4

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Abbreviations

AS	Active surveillance
CT	Computed tomography
FNA	Fine-needle aspiration
MRI	Magnetic resonance imaging
RCC	Renal cell carcinoma
RTB	Renal tumour biopsy
SRM	Small renal mass

Key Messages

- The increased in the detection of small renal masses has been associated with a concomitant rise in the rate of benign renal tumour treatment.
- Pretreatment biopsy is the only way to reduce unnecessary treatment. Renal tumour biopsy (RTB) is cost-effective and safe, with a significant complication rate of <1%.
- RTBs have been associated with a high diagnostic yield (up to 94.3%) and accuracy, with high concordance rates of histologic subtypes.
- Although RTBs have traditionally been deficient with regard to grade identification, contemporary studies have demonstrated a high concordance rate with definitive pathology when a two-tier grading system was used.
- A larger tumour size, solid or exophytic tumour component, the use of core needle biopsies and the use of large-bore needles (≤18 gauge) have all been associated with higher rates for diagnostic biopsy.

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4.1 Introduction

The increasing use of abdominal computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound has led to an increase in the incidental detection of solid small renal masses (SRMs) [1]. This has been associated with a concomitant increase in the detection of benign SRMs [2, 3]. Although radiological imaging is useful to identify fat-containing angiomyolipomas [4], there is currently no reliable imaging modality to define the histology of fat-poor solid lesions [5]. Traditionally the trend has been to diagnose all enhancing SRMs as possible renal cell carcinomas (RCCs) and to obtain histologic confirmation after treatment by surgery or biopsy at the time of ablation. However, over the last decades, renal tumour biopsies (RTBs) have been proposed as an alternative to establish the histological diagnosis preoperatively and as a way to decrease overtreatment of benign SRMs. Although the role of RTBs has previously been limited due to a high rate of non-diagnostic biopsies [6], contemporary studies suggest that they are becoming more reliable. Hence, RTB is gaining popularity in the treatment decision algorithms of patients with indeterminate solid SRMs.

We will review the technical considerations, outcome, safety and role of RTB performed for the preoperative identification of the aetiology of SRMs.

4.2 Indications and Role of Renal Tumour Biopsies

Traditionally, the role of RTB in the evaluation of renal masses was quite limited due to concerns of low diagnostic rates, lack of correlation with surgical pathology, safety concerns and controversy about clinical utility. Thus, RTB was primarily limited to the identification of lesions suspicious of a haematological malignancy (such as lymphoma), infection or inflammation or in cases where metastatic renal cancer was suspected. More recently, RTB is increasingly considered by the urologist to define the histology of SRMs before treatment [7]. The increase in the detection of SRMs has been associated with a concomitant increase in benign tumours [2, 3]. It is now recognized that up to 30% of SRMs are benign [2, 3]. Surgical treatment of these benign renal tumours is generally considered as overtreatment. Therefore, RTB has been proposed as one way to potentially reduce overtreatment. Although this indication is not universally accepted, RTB has also been proposed prior to thermal ablation therapy to help define treatment success and interpret the need for further treatment or intervention [8, 9]. Most biopsies continue to be performed at the time of ablation, not before. Furthermore, it is now recognised that more and more SRMs that are biopsy-proven small RCCs are diagnosed in the elderly population who may have comorbidities. RTBs can provide useful information for these patients who are not ideal surgical candidates as well as in healthy patients who are considering active surveillance (AS) as their treatment of choice [9]. Although it has been shown that the majority of SRMs are of low nuclear grade [10], a conservative approach might not be recommended if high-risk adverse features are proven on biopsy. Finally, there is emerging information about the natural history of different subtypes of RCC, and it is possible that some histologies would be best managed by initial AS, even in younger patients.

4.3 Penetrance of RTB in Daily Practice

Despite the potential benefits, there has been a slow adoption of RTB in clinical practice. In a survey of members of the Endourological Society, Barwari et al. [11] reported, in 2012, that the majority of responders (73%) never or rarely perform biopsies and only 9% of responders recommend biopsies in more than 25% of the cases. More recently, a Surveillance, Epidemiology, and End Results-Medicare (SEER) database study has shown approximately 20% of patients diagnosed with renal carcinoma underwent a RTB before instituting therapy [12]. They also demonstrated an increase in the uptake of RTB over time with a rate of 30.3% in 2007. However, the increase was primarily seen among patients with metastatic disease and among patients undergoing percutaneous ablative therapy, whereas utili-

zation in patients with localized disease has not appreciably increased over the study period. As previously stated, several concerns might explain this delay in uptake among urologists. However, several contemporary studies have addressed these concerns which may lead to evolving perceptions in the future [13–18].

4.4 Technical Considerations

4.4.1 Fine-Needle Aspiration Versus Needle Core Biopsies

RTBs have classically been performed using two methods for obtaining renal tissue samples, fine-needle aspiration (FNA) or needle core biopsy. FNA is a process through which the tumour cellular elements are aspirated during multiple needle passes through the tumour. Needle core biopsies are performed through a coaxial sheath using needles of different sizes to provide limited number of cores. Thus, theoretically, FNA provides a more extensive sampling of the tumour but with tissue of lesser quality.

However, FNA yields lower diagnostic rates when compared to core biopsies [19]. Moreover, although FNA may provide a more extensive sampling of the lesion, it does not allow the same histologic examination as core biopsy does [19]. It has been suggested that due to their differing sampling techniques, adding FNA to core biopsy could help improve diagnostic yield, but this remains controversial and we do not routinely do both [19].

4.4.2 Image Guidance

RTB is typically performed as an outpatient or short-stay procedure under local anaesthetic with ultrasound or CT guidance. MRI guidance has also been reported [20]. There are currently no data suggesting superiority of one type of image guidance over another. In the largest single-institution study reported, ultrasound guidance was associated with greater diagnostic odds on univariate analysis; however, it was not shown to be a significant predictor on multivariate analysis after adjusting for other clinical characteristics [13]. Compared to CT, ultrasound has the advantages of real-time visualisation of the lesion during biopsy, lower cost and avoidance of ionizing radiation. Nonetheless, CT guidance does have some advantages over ultrasound guidance. It has an excellent spatial resolution, better needle visualization and improved avoidance of necrotic area. Given the evidence, it seems that the type of imaging used depends more on the operator preference, availability of guiding method as well as patient and tumour characteristics.

4.4.3 Needle Size

Several studies have investigated the effect of needle size on the outcome of RTBs [21–24]. Breda et al. compared the accuracy of 14-, 18- and 20-gauge needle biopsies in a prospective study and concluded that larger bore needles (14- and 18-gauge) were the most accurate in determining the histological diagnosis [21]. Similar results were obtained when 14- and 18-gauge needles were compared. Several other studies have confirmed the lack of benefit of using larger bore needles [22, 23]. As a result, most centres now commonly use 18-gauge needles for RTBs.

Another study, although limited by its small sample size, has also suggested that the use of a coaxial biopsy sheath improves biopsy outcome and increases the standardisation of tissue samples [24]. The sheaths have also been proposed as factor in the elimination of tumour seeding [10]. Despite the lack of strong evidence supporting the use of sheaths, it seems reasonable to perform RTB through them. Nonetheless, some outpatient, ultrasound-guided biopsies are being done without a sheath due to the port size of the US transducer without any reported seeding [25].

4.4.4 Number of Cores

To date, the optimal number of cores to be taken at the time of biopsy has not been defined. It has been suggested that increasing the number of

cores improves the diagnostic yield [26]. We have found a 90.0% diagnostic rate with a median of three cores taken at the time of biopsy [13]. However, the number of cores taken was not shown to be associated with higher diagnostic rate. Similarly, other studies have failed to demonstrate such an association [17]. Despite these results, it seems reasonable that increasing the number of cores taken will increase the amount of tissue available for diagnosis and, as a result, increase the odds of obtaining a diagnosis. It has recently been recommended by a body of experts in the field that at least two cores should be sampled during RTB with the aim to obtain optimal quality of tissue to maximize diagnostic yield [27].

4.5 Diagnostic Accuracy

4.5.1 Diagnostic Yield

One of the major criticisms of the clinical utility of RTB was the low diagnostic rates in initial series either from inadequate tissue sampling or inability to correctly interpret the tissue sampled [6, 28]. However, with refinement of biopsy techniques and increased experience, the outcomes of RTB in more recent series have greatly improved. The diagnostic yields in most recent series have varied from 62.4 to 94.3% [5, 13–15, 17–19, 22, 29–45]. Table 4.1 summarizes the studies on RTB published after 2000 with a sample size greater than 50 biopsies.

In our own experience, we have found a 90.0% diagnostic rate when RTBs were performed for pretreatment characterisation of solid SRMs [13]. Importantly, for the 53 non-diagnostic biopsies, a repeat biopsy yielded a diagnosis in 83.6% of the cases, of which 40.0% were benign. A non-diagnostic biopsy is not a surrogate for benign histology. Given the relatively high diagnostic rate as well as the high benign rate, it seems worthwhile, in our opinion, to consider the re-biopsy of a SRM after a non-diagnostic result. When including initial and repeat RTB, we were therefore able to obtain a diagnosis in 496 of 529 SRMs for an overall diagnostic rate of 93.8% [13].

4.5.2 Diagnostic Accuracy for Malignancy

The diagnostic accuracy of RTB to differentiate benign and malignant tumours is generally high and ranges from 86 to 100%, with a specificity nearing 100% in most recent series [10]. One caveat is that the majority of patients diagnosed with benign lesions were not treated following the diagnosis [13–18, 46], and as such, one cannot be certain that these were indeed benign in nature.

4.5.3 Histologic Accuracy

Recent studies have reported that RTB results have high rates of concordance with surgical pathology and are usually able to provide sufficient information to provide additional prognostic value to the patients [10, 27]. In the majority of contemporary studies, the concordance rates exceed 80% with rates as high as 98% [10]. However, at least in our experience, RTB did not fare as well when specifically trying to differentiate between papillary subtypes, with agreement rate nearing 53% [13]. Moreover, there continues to be a challenge when trying to distinguish oncocytomas from chromophobe subtypes. It has been suggested that the use of additional staining and immunohistochemistry may reduce this diagnostic dilemma [27]. Using these techniques, we have found a 100% concordance rate when differentiating oncocytomas from chromophobe tumours, although the vast majority of patients diagnosed in our series with an oncocytic tumour did not have confirmatory surgical extirpation of their lesions [13].

4.5.4 Grade Accuracy

RTBs have generally performed poorly or at least not reliably enough to accurately identify nuclear grading. The reported accuracy of RTB-based grading tumours ranges from 46 to 76% [10, 13, 27]. However, this may be improved by using a simplified two-tier grading system

Table 4.1 Percutaneous renal tumour biopsy studies published since 2000 with sample size greater than 50 biopsies

Study	Publication year	Tumours/ biopsy, n	Mean tumour size (cm)	Diagnostic, n (%)	Non-diagnostic, n (%)	Cancer, n (%)	Benign, n (%)
Lechevallier et al. [29]	2000	71	4.0	56 (78.9)	15 (21.1)	48 (85.7)	8 (14.3)
Richter et al. [30]	2000	205	n/a	128 (62.4)	77 (37.6)	49 (38.3)	79 (61.7)
Rybicki et al. [22]	2003	99	n/a	90 (90.9)	9 (9.1)	86 (95.5)	4 (4.5)
Neuzillet et al. [31]	2004	88	2.8	80 (90.9)	8 (9.1)	66 (82.5)	14 (17.5)
Blumenfeld et al. [32]	2010	81	5.3	79 (97.5)	2 (2.5)	78 (98.7)	1 (1.3)
Vasudevan et al. [33]	2006	100	<5.0	70 (70.0)	30 (30.0)	47 (67.1)	23 (32.9)
Maturen et al. [18]	2007	152	4.1	146 (96.1)	6 (3.9)	85 (58.2)	61 (41.8)
Beland et al. [5]	2007	58	3.1	52 (89.7)	6 (10.3)	38 (73.1)	14 (26.9)
Lebret et al. [34]	2007	119	3.3	94 (79.0)	25 (21.0)	70 (74.5)	24 (25.5)
Hellburn et al. [35]	2007	93	2.9	82 (88.2)	11 (11.8)	78 (95.1)	4 (4.9)
Somani et al. [36]	2007	70	n/a	61 (87.1)	9 (12.9)	44 (72.1)	17 (27.9)
Rybikowski et al. [37]	2008	70	<4.0	56 (80.0)	14 (20.0)	52 (92.9)	4 (7.1)
Schmidbauer et al. [38]	2008	122	3.9	115 (94.3)	7 (5.7)	89 (77.4)	26 (22.6)
Shannon et al. [39]	2008	235	2.9	184 (78.3)	51 (21.7)	138 (75.0)	46 (25.0)
Thuillier et al. [40]	2008	53	2.6	41 (77.5)	12 (22.5)	32 (78.0)	9 (22.0)
Volpe et al. [15]	2008	100	2.4	84 (84.0)	16 (16.0)	68 (81.0)	16 (19.0)
Wang et al. [41]	2009	110	2.7	100 (90.9)	10 (9.1)	65 (65.0)	35 (35.0)
Leveridge et al. [14]	2011	345	2.6	278 (80.6)	67 (19.4)	221 (79.5)	57 (20.5)
Veltri et al. [42]	2011	150	3.4	129 (86.0)	21 (14.0)	97 (75.2)	32 (24.8)
Menogue et al. [17]	2012	268	2.5	214 (80.0)	54 (20.0)	158 (74.0)	56 (26.0)
Breen et al. [43]	2013	135	n/a	120 (88.9)	15 (11.1)	97 (80.8)	23 (19.2)
Davis et al. [44]	2013	276	n/a	212 (76.8)	64 (23.2)	207 (97.6)[a]	5 (2.4)
Park et al. [19]	2013	59	2.4	48 (81.4)	11 (18.6)	37 (77.0)	11 (23.0)
Salem et al. [45]	2013	144	2.4	125 (86.9)	19 (13.1)	107 (84.9)	18 (15.1)
Richard et al. [13]	2014	529	2.5	476 (90.0)	53 (10.0)	353 (74.2)	123 (25.8)
Total	—	3732	2.9	3120 (83.6)	612 (16.4)	2410 (77.2)	710 (22.8)

[a]Includes malignant tumours or potentially malignant tumours (oncocytic neoplasms)

which may have a superior prognostic value [47]. When using this simplified grading system, contemporary studies have shown that RTB accuracy ranges from 64% to nearly 95% [10, 13]. The discrepancy between the biopsy grade and the final surgical pathology may be in part explained by the well-known heterogeneity of renal tumours [48]. This phenomenon may account for the tendency of RTBs to undergrade when compared to final surgical pathology, although this is far less likely when the two-tier system is used [10, 13, 27, 32]. The utility of nuclear grading on RTB remains controversial. Moreover, in view of the current ongoing debate over the prognostic significance of nuclear grading in non-clear cell histology subtype [49], many centres, including ours, have now chosen to apply the grading system to clear cell histology subtype only. Regardless, the authors feel that the identification of high-grade components carries a very high positive predictive value and helps better counsel patient with regard to treatment choice.

4.5.5 Predictors of a Diagnostic Biopsies

A few factors have been reported as being associated with greater odds of obtaining a diagnostic biopsy. Although further studies will be required to confirm these factors, the available information is useful when counselling patients about the diagnostic rate of RTB. Physicians and patients should be aware of these predictors when considering RTB. These will be reviewed below.

4.5.5.1 Tumour Size

Tumour size has been associated with RTB outcome in the majority of studies evaluating the influence of tumour dimension [13, 14, 23, 41, 44]. Generally, larger tumours have been associated with greater diagnostic yield. We have observed that the odds ratio (OR) for a diagnostic outcome was 1.66 (95% confidence interval [CI]: 1.12–2.46) for every 1 cm increase in tumour size (p = 0.012) after adjusting for age, exophytic appearance, type of imaging used and number of previous RTB performed by the provider, among patients undergoing an initial RTB (n = 529).

4.5.5.2 Lesion Location

In general, biopsies done for endophytic lesions or for lesions located anteriorly near the hilum or on the upper pole are thought to be technically more challenging. However, very few studies have evaluated the outcome of RTB with relation to the lesion's characteristics or exophytic appearance. The presence of an upper pole lesion was found to be significantly associated with the biopsy's outcome in a study by Leveridge et al., but not on multivariate analysis, and this was confirmed by subsequent studies [13, 14]. Similarly, the laterality of the biopsied kidney does not seem to influence the outcome [13]. However, it has been demonstrated with multivariable analysis that RTB of exophytic lesions was more likely to be diagnostic than RTB in endophytic ones (OR: 2.35, 95%CI: 1.23–4.47; p = 0.009) [13]. To our knowledge, whether the presence of an anterior tumour is less likely to be diagnostic than a posterior lesion is yet to be evaluated.

4.5.5.3 Solid Versus Cystic Components

Although the majority of RTBs are performed for the preoperative identification of solid lesions, several reports have proposed their use in the assessment of complex cystic renal masses [14, 15, 44]. Several investigators have suggested that the rate of adequate tissue sampling with core biopsy was as high in cystic lesions as in solid lesions. However, there is now limited evidence that RTB of complex cystic lesions is significantly less likely to be diagnostic than RTB performed in solid lesions [14, 15]. Based on the Leveridge et al. conclusions, the observed OR for a diagnostic biopsy was 13.9 (95%: 3.78–50.7; $p < 0.0001$) for a solid versus cystic lesion component [14]. Nonetheless, Richter et al. did find that 89.4% of 227 Bosniak II/III lesions were accurately classified using a combination of FNA cytology and RTB. Among these patients, 39% avoided unnecessary surgery following a benign diagnosis [30]. Moreover, a larger study evaluating the impact of core biopsy and FNAs on 199

Bosniak IIF or III cystic lesions demonstrated an 87.9% diagnostic rate. More importantly, invasive procedures were avoided in 70% of the patients following the biopsy [50].

The discrepancy between the outcomes of RTB in the evaluation of complex cystic mass highlights the need for additional well-powered prospective studies re-examining its role in this context. Meanwhile, given the current evidence of lower diagnostic rate and potential for seeding tumour cells from cyst rupture, many urologists are limiting the indication of RTB to Bosniak IV cysts, where a clear enhancing and solid lesion is visible within the cyst on imaging [10]. As a result of the evidence, the decision to proceed to a RTB in patients with complex cystic lesions should be made on an individual basis. Moreover, it seems worthwhile to consider a combination of core biopsy and FNA when opting for RTB in the work-up of complex cystic masses.

4.5.5.4 Patient Characteristics

We have evaluated several patient characteristics as potential predictors of RTB outcomes [13]. Although the patient's body habitus may potentially influence the RTB outcome, the literature is yet to support this hypothesis. To our knowledge, although several other patient characteristics have been evaluated (age, gender, performance status), none have been reported to be associated with biopsy outcome.

4.6 Impact on Clinical Management

Non-adopters of routine RTBs have long argued that results will not significantly alter clinical management. However, recent studies have suggested this is not the case. We have demonstrated that nearly 41% of our cohort avoided definitive treatment following biopsy either because they were found to have a benign tumour, favourable histology or because the RTB confirmed the presence of metastatic disease of another primary origin [13]. Similarly, Maturen et al. have shown that the biopsies significantly impacted on clinical management in 60.5% of their cohort which was defined as a change between surgery and no surgery [18]. Although clinical judgement remains important, a risk stratification algorithm to help direct management following RTBs has been proposed [46]. Using their Michigan algorithm (Fig. 4.1) which incorporates tumour histology and size, depth of tumour invasion and patient's performance status, Halverson et al. have demonstrated that biopsies were 96% sensitive and 100% specific in correctly assigning patients to intervention versus active surveillance. However, longer prospective studies will be required to validate this strategy.

4.7 Complications

In the past, biopsied patients were considered at high risk of complications including tumour seeding and bleeding. However, recent studies have shown that despite the utilisation of large-bore needles for core biopsy and multiple needle passes for each RTB, the rate of adverse events is low [10, 13, 27]. Moreover, these complications are usually self-limiting and low grade in nature. Minor bleeding is the most commonly reported adverse event. In our experience, there was an 8.5% complication rate following the biopsy. The

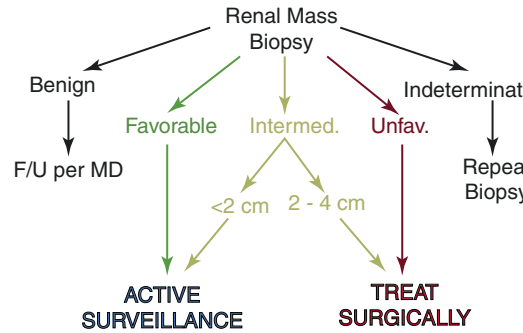

Fig. 4.1 Proposed simplified biopsy directed management algorithm designating active surveillance vs. treatment based on mass size and histological risk category. Reprinted with permission from Elsevier from The Journal of Urology, Volume 189 (2), Schuyler J. Halverson, Lakshmi P, et al., Accuracy of Determining Small Renal Mass Management with Risk Stratified Biopsies: Confirmation by Final Pathology. Pages 441-446. Copyright (2013)

majority of these were bleeding-related events and were for the most part diagnosed on routine post-procedure imaging. Most importantly, only one patient (0.2%) has required angioembolization [13].

Only six cases of tumour seeding along the needle track have been reported and all were prior to 2001 [34]. None have been reported despite the increase in RTBs [10]. One possible explanation is that the use of the coaxial sheath in more recent series has decreased the direct contact of the biopsy needle with the surrounding abdominal tissue and, as a result, has further decreased the risk of seeding. Patients should be cautioned that reports and commentary available on the internet are frequently not dated and may not reflect recent experience.

Other complications are extremely rare [10]. Rates of significant clinical pneumothorax are reported to be present in less than 1% of the cases and even rarer when a subcostal approach is chosen. Overall, the reported risk of complications associated with RTBs is low and should not be a deterrent to recommend a biopsy.

4.8 Cost-Effectiveness

In addition to being safe, reliable and associated with potential decreases in overtreatment rates, cost-effectiveness studies have also suggested that biopsy is a cost-effective procedure [51, 52]. Using decision-analytic Markov models, two studies have evaluated the cost-effectiveness of RTB over upfront surgery. They found that the use of biopsies to triage patients to surgery resulted in similar life expectancies for an empirical surgical approach compared to a biopsy-directed nonoperative approach. Their results also supported the use of RTBs as a cost-effective approach.

4.9 Limitations

Although we have detailed the safety and benefits of RTBs, there are some limitations of biopsy. Firstly, the infrequent hybrid tumours cannot be adequately defined using RTBs [53]. It is possible to miss the malignant portion of a hybrid tumour and misclassify the lesion as being benign. The only way RTB would deliver the correct diagnosis of a heterogeneous lesion is if the biopsy targets the hybrid area [54]. Hybrid tumours have previously been reported to present in up to 18% of oncocytomas diagnosed following RTB [53], although this has not been our experience [55]. We believe that patients should be made aware of this risk when opting for surveillance following diagnosis.

Another limitation of RTB may occur in patients with multifocal renal lesions. Knowing the histology of one tumour does not reveal information about the histology of the other synchronous tumours [38]. Thus, in patients with multiple lesions in which RTBs are being considered, each lesion should be biopsied to identify their respective histology.

4.10 Future Role

The indications of RTBs continue to expand. Predominantly performed for SRMs to aid in diagnosis and subsequent management, larger tumours >4 cm are also being subject to RTBs. Benign oncocytomas are known to grow at a similar rate as RCC and can often present with tumour sizes of >4 cm. In an unfit patient with a large benign oncocytoma, one could adopt a conservative approach based on the biopsy findings [55].

Technical improvements continue to evolve. Volpe and colleagues showed that the use of full-core needles as opposed to Tru-Cut needles (standard in most centres) was potentially associated with a higher diagnostic yield for tumour histological type and grade, with a superior yield of pathologic specimen adequacy [56].

Research continues on molecular profiling of RTBs in an attempt to not only improve diagnostic accuracy and improve histological subtyping and grading but also to identify molecular biomarkers to aid in predicting prognosis. Preliminary studies have shown that significant differences in DNA methylation levels exist at

specific sites on the human genome, and these have been proposed as a means to differentiate cancer from benign tissue [57].

MicroRNA (miRNA) signatures have also been shown to accurately distinguish between histological subtypes using quantitative reverse transcription-polymerase chain reaction analysis with miRNA-specific primers. Sensitivities of 97–100% have been attained in diagnosing normal tissue from RCC, as well as histological subtypes [58], and this technique can be utilized with RTBs.

Another recent study of image-guided SRM biopsies showed that genomic alterations are detectable by array comparative genomic hybridization (aCGH) using a targeted oligonucleotide microarray in over 90% of specimens, hence augmenting histological findings from RTBs. Importantly, this preliminary study showed clonal genomic alterations associated with malignancy in two out of three low-grade oncocytic neoplasms [59]. Further validation is required, and this may pave the way in the future for a more definitive distinction between benign and malignant oncocytic lesions. However, one must be cognisant of the fact that regional variations in gene mutations exist within a tumour, and a single-site needle biopsy may not capture the broader tumour landscape when validating biomarkers [60].

Conclusion

Despite compelling evidence in favour of RTB, critics continue to argue against routine RTB of SRMs because of uncertainty related to diagnostic rates, concordance with final pathology, safety concerns and lack of impact on the clinical management. Several contemporary studies have demonstrated that these concerns are exaggerated. These studies have shown that RTBs can now be performed with low morbidity, with a good diagnostic yield and with good accuracy for malignancy and histology, especially in centres of expertise. Moreover, in addition of decreasing overtreatment rates, RTBs have also been shown to be a cost-effective approach. Given the accumulation of evidence supporting RTBs, we believe that they should be considered as the initial step in the management of patients with indeterminate SRMs in whom a therapeutic approach is being considered. In an era where overdiagnosis and overtreatment of cancers is gaining attention, we believe that the utilisation of RTBs will lead to personalisation of care and limit unnecessary and costly interventions. However, RTBs are not indicated for healthy patients who are unwilling to accept the uncertainty associated with this procedure or for patients who will only consider active surveillance regardless of biopsy results.

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The Role of Active Surveillance for Small Renal Masses

5

Alessandro Volpe

Abbreviations

CCI	Charlson comorbidity index
CT	Computed tomography
FNA	Fine needle aspiration
RCC	Renal cell carcinoma
SRM	Small renal mass

Key Messages

- Increases in the incidence of renal cell carcinoma have been mainly due to increased diagnosis of small renal masses (SRMs).
- Recent data show that the risk of progression to metastatic disease and cancer-related mortality in SRM is low.
- For patients with significant comorbidities or limited life expectancy, active surveillance can be proposed as a reasonable treatment option.
- Active surveillance uses serial abdominal imaging to monitor the growth rate and clinical behaviour of a SRM with delayed active treatment reserved only for those tumours which show a fast growth or clinical progression.
- Active surveillance requires an adequate and thorough patient counselling, a precise organization of follow-up and a good patient compliance.
- In experienced centres, percutaneous renal tumour biopsies of SRM have been shown to be safe with a good detection rate and can provide important information for treatment decisions.

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5.1 Introduction

The incidence of renal cell carcinoma (RCC) has been steadily growing in the last decades, largely due to a wider use of modern and accurate abdominal imaging modalities. The increase in incidence is mainly due to the increased diagnosis of localized renal tumours [1]. In fact, most RCCs are today discovered incidentally as small renal masses (SRMs) in asymptomatic patients. The lesions discovered incidentally are on average smaller and of a lower stage compared to those detected in symptomatic patients [2]. In addition, a significant number of small, asymptomatic tumours appear to be benign. Frank et al. have reviewed the histology of 2935 renal tumours operated at Mayo Clinic, observing a significant increase in the probability of benign histology with decreasing tumour size. Overall, 30% of tumours <4 cm were histologically benign, and more than 87% of clear cell RCC tumours were low grade [3]. Many authors have also shown that small, incidental tumours are characterized by a better survival [2, 4]. The first evidence of an association between tumour size and prognosis was provided by Bell, who noticed an increased incidence of metastases in patients in whom a RCC > 3 cm was found at autopsy [5].

5.2 Natural History of Small Renal Tumours

SRMs are generally surgically removed soon after diagnosis. For this reason, their natural history has only recently been better defined. In 1995 Bosniak et al. retrospectively examined the imaging of 40 incidental renal masses (<3.5 cm) which had been followed without active treatment for an average of 3.2 years. Twenty-six tumours were eventually removed after an average of 3.8 years, and 84.6% of them were histologically RCCs. Variable tumour growth behaviours were observed, and the overall mean linear growth rate was 0.36 cm/year (0–1.1 cm/year). Nineteen tumours grew less than 0.35 cm/year, and no patient developed metastatic disease [6]. It is important to note that these patients were reviewed at the time of surgery so that there may have been a bias towards faster growth.

The first prospective study of observation of SRMs was conducted at the University Health Network in Toronto. The authors followed over time, with serial abdominal imaging, 32 incidentally diagnosed, <4 cm renal masses in patients who were elderly or unfit for surgery. Twenty-five tumours were solid and seven complex cystic (four Bosniak III and three Bosniak IV). The patients were prospectively followed with serial abdominal imaging for a mean of 27.9 months (range 5.3–143 months), and each mass had at least three follow-up measurements. Tumour volume in addition to single and bi-dimensional diameters was calculated from each follow-up image or report. Nine masses in eight patients were surgically removed after an average of 38 months of follow-up because of the surgeon's concern or the patient's anxiety that the tumour was enlarging. All tumours were clear cell RCCs except one, which was an oncocytoma. Overall average growth rate was 0.1 cm/year and was not associated with either initial size ($p = 0.28$) or mass type ($p = 0.41$) (Fig. 5.1). Seven masses (22%) reached 4 cm in diameter after 12–85 months of follow-up. Eight (25%) doubled their volumes within 12 months. Overall, 11 (34%) fulfilled one of these two criteria of rapid growth. No patient progressed to metastatic disease, while two patients died of unrelated causes [7]. Several other series of active surveillance of SRMs have been subsequently published, showing similar results (Tables 5.1 and 5.2).

A meta-analysis published in 2006 included 234 renal masses followed with active surveillance in eight institutions in North America and Japan. The average tumour diameter was 2.6 cm and the mean follow-up 34 months. The average tumour growth rate was 0.28 cm/year. Histological confirmation was available in 46% of cases, and 92% of these SRMs were found to be RCCs. This meta-analysis indicated that size at diagnosis does not correlate with tumour growth rate ($p = 0.46$) [9].

Another pooled analysis of studies of active surveillance has recently included 18 series with a total of 880 patients and 936 renal masses with an average diameter of 2.3 cm at diagnosis. With a mean follow-up of 33.5 months, the average growth rate was 0.31 cm/year. When histological

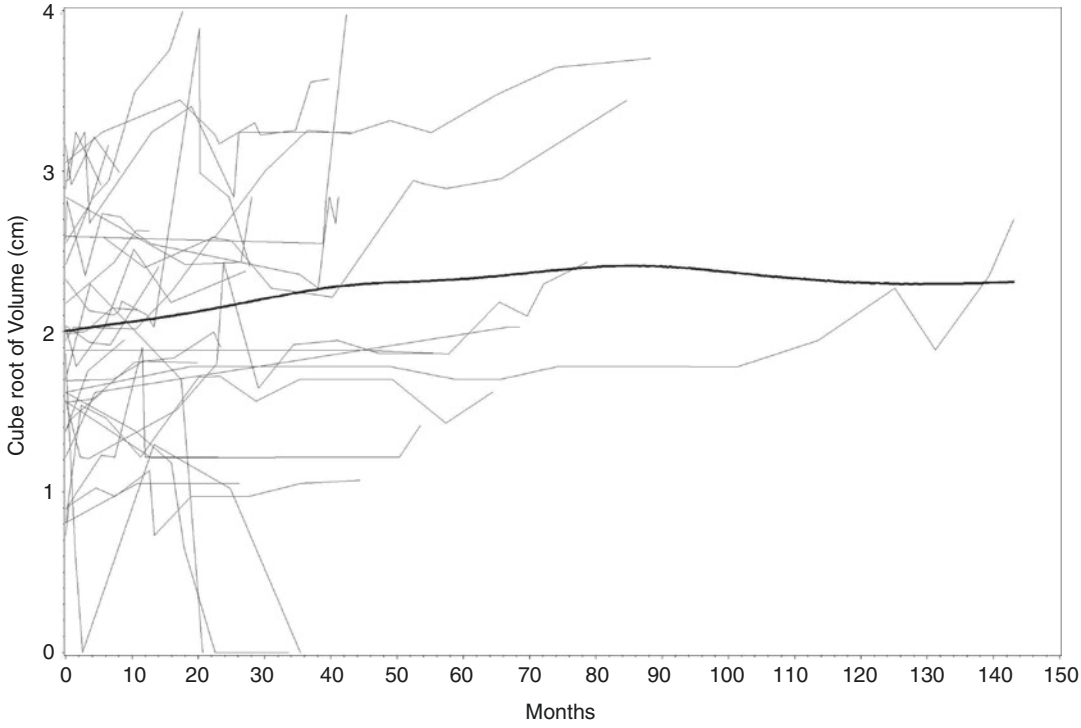

Fig. 5.1 Growth pattern of 32 small renal masses in active surveillance (*grey dotted lines*). The *black line* represents the average growth rate (from Volpe et al. [7])

characterization was obtained, 88% of renal masses were found to be RCCs. Sixty-five tumours (23%) showed no growth during the surveillance period [10].

The evidence resulting from these studies clearly indicates that progression to metastatic disease is rare during active surveillance (1–2% of cases) [9, 10]. Smaldone et al. observed that the probability of progression to metastatic disease is significantly higher for tumours with greater diameter at diagnosis (4.1 ± 2.1 cm vs. 2.3 ± 1.3 cm, $p < 0.001$) and with a faster growth rate during surveillance (0.8 ± 0.7 cm/year vs. 0.3 ± 0.4 cm/year, $p < 0.001$) [10].

Most available studies of active surveillance are retrospective, have a relatively short follow-up and include a relatively small number of patients. However, the results of two large, prospective and multi-institutional clinical trials have been recently published. These studies confirmed the safety and good oncological outcomes of active surveillance of SRMs with short- to intermediate-term follow-up [13, 14].

The first results of a prospective phase II study including 209 SRMs in 178 elderly or infirm patients from eight Canadian academic centres were reported by Jewett et al. in 2011. At a mean follow-up of 22 months, the tumour growth rate was on average 0.13 cm/year, and 37% of SRMs showed no growth during follow-up. Percutaneous biopsy was proposed at diagnosis and was eventually performed in 101 cases (48.3%). The growth rate of histologically confirmed malignant lesions was not statistically faster compared to the growth rate of histologically confirmed benign tumours. Very importantly, progression to metastatic disease was observed in only two cases (1.1%) [13]. A further analysis on this cohort of patients revealed that patient age, symptoms at diagnosis, tumour pattern and maximum diameter were not predictors of the growth of SRMs [15].

Finally, Pierorazio et al. recently reported the results of a multicentre clinical trial based on the DISSRM (Delayed Intervention and Surveillance for Small Renal Masses) registry. This study

Table 5.1 Mean growth rate and progression to metastatic disease in the largest series of active surveillance of SRMs

	Cases	Study design	Mean tumour size (cm)	Mean follow-up (mos)	Mean growth rate (cm/year)	Progression to metastasis (%)
Bosniak et al., Semin Urol Oncol (1995)	40	Retrosp. Mono	1.73	39	0.36 (0–1.1)	NA
Volpe et al., Cancer (2004)	32	Prosp. Mono	2.48	27.9	0.1 (NA)	0
Kassouf et al., J Urol (2004)	24	Retrosp. Mono	3.27	31.6	0.09 (0–1.2)	0
Kato et al., J Urol (2004)	18	Retrosp. Mono	1.98	22.5	0.42 (0.08–1.6)	NA
Wehle et al., Urology (2004)	29	Retrosp. Mono	1.83	32	0.12 (NA)	0
Kouba et al., J Urol (2007)	46	Retrosp. Mono	2.92	35.8	0.39 (0–3.51)	0
Abouassaly et al., J Urol (2008)	110	Retrosp. Mono	2.5	24	0.26 (0–3.26)	0
Crispen et al., Cancer (2010)	173	Retrosp. Mono	2.5	31	0.28 (−1.4–2.47)	2 (1.3)
Rosales et al., J Urol (2010)	223	Retrosp. Mono	2.8	35	0.34 (0.29–2.3)	1 (0.5)
Haramis et al., Urology (2011)	44	Retrosp. Mono	2.67	77.1	0.15 (0–1.73)	0
Smaldone et al., Cancer (2012)	880	Pooled analysis	2.3	33.5	0.31 (−1.4–2.5)	18 (2)
Jewett et al., Eur Urol (2011)	178	Prosp. Multi	2.1	28	0.13 (NA)	2 (1.1)
Pierorazio et al., Eur Urol (2015)	223	Prosp. Multi	1.9	24	0.11 (−1.1–0.41)	0

Retrosp. retrospective study, *Prosp.* prospective study, *Multi* multi-institutional study, *Mono* single institutional study, *NA* not available

included 497 patients with SRMs, of which 223 (45%) were followed with active surveillance and the remaining underwent active treatment. The study was prospective, but not randomized, and the median follow-up was 2.1 years. In the active surveillance group, a rapid growth rate led to the indication of a deferred surgical or ablative treatment in only 36 cases (16.1%). No patient developed metastases during active surveillance (cancer-specific survival 100%), while the overall survival in this group of patients was, respectively, 96% and 75% at 2 and 5 years compared to 98% and 96% in the active intervention group [14]. Further analysis based on the DISSRM registry has recently shown that patients on active surveillance present better preservation of renal function assessed by eGFR compared to patients who underwent radical nephrectomy, but not to those who underwent partial nephrectomy [16].

5.3 Natural History of cT1b-cT2 Renal Tumours

The results of few series of active surveillance for larger renal masses have also been reported. Lamb et al. assessed the natural history of 36 renal tumours with a median tumour size of 6.0 cm (range 3.5–20 cm) in elderly patients with severe comorbidities or high risk of postoperative dialysis. The mean patient age was 76.1 years, and the median follow-up was 24 months. Thirteen patients (36.1%) died of other causes after an average of 9 months from diagnosis of

Table 5.2 Pathology of SRMs in the largest series of active surveillance

	Cases	Available pathology (%)	RCC at pathology (%)
Bosniak et al., Semin Urol Oncol (1995)	40	26 (65)	22 (85)
Volpe et al., Cancer (2004)	32	9 (28)	8 (89)
Kassouf et al., J Urol (2004)	24	4 (15)	4 (100)
Kato et al. J Urol (2004)	18	18 (100)	18 (100)
Wehle et al., Urology (2004)	29	4 (14)	3 (75)
Kouba et al., J Urol (2007)	46	14 (30.4)	12 (87)
Abou Youssif et al., Cancer (2007)	44	8 (23)	6 (75)
Abouassal yet al., J Urol (2008)	110	9 (8)	3 (33)
Crispen et al., Cancer (2010)	173	68 (39)	57 (84)
Rosales et al., J Urol (2010)	223	40 (18)	37 (92.5)
Haramis et al., Urology (2011)	44	17 (38.6)	17 (100)
Jewett et al., Eur Urol (2011)	178	101 (48.3)	56 (55)
Pierorazio et al., Eur Urol (2015)	223	32 (14.3)	13 (41)

NA not available

their renal tumour, and no cancer-specific death was observed. Only one patient developed metastatic disease 132 months after diagnosis and was still alive at 136 months. The mean tumour size was roughly unchanged in most patients during the follow-up period [17]. More recently, Mues et al. reported the outcomes of active surveillance in 36 patients with 42 localized renal tumours larger than 4 cm. About 52.8% of these patients had severe comorbidities with a Charlson comorbidity index (CCI) ≥ 3, while only 25% of them were symptomatic at diagnosis. The mean patient age was 73.8 years, the mean tumour size was 7.13 cm and the median linear growth rate was 0.57 cm/year. Percutaneous renal biopsies were performed in 12 patients, and pathology revealed 10 clear cell RCC, 1 chromophobe RCC and 1 undifferentiated tumour. Three patients with a fast tumour growth rate were treated with delayed laparoscopic radical nephrectomy. Pathology showed clear cell RCC in all cases. Overall, only two patients (5.6%) progressed to metastases, and no cancer-related deaths were observed [18].

Another recent report from the United States assessed a cohort of 68 patients with 72 contrast-enhancing cT1b-cT2 renal tumours. The patients were managed expectantly with active surveillance for at least 6 months from diagnosis. The mean patients' age was 69 years, the median CCI was 3 and the mean tumour size at presentation was 5.3 cm. The mean linear growth rate was 0.44 cm/year. The mean R.E.N.A.L. nephrometry score was 8.7 ± 1.6, suggesting anatomically intermediate to complex renal tumours. Renal tumour biopsies were performed in 21 patients (31%). At a mean follow-up of 39 months, 45 patients remained on surveillance, while 23 underwent delayed surgical intervention because of fast tumour growth, development of tumour-related symptoms, patient or physician choice. Patients who stayed on active surveillance were older (77 vs. 60 years, $p = 0.0002$) and had slower linear growth rate (0.37 cm/year vs. 0.73 cm/year, $p = 0.02$) compared to those who underwent delayed intervention. Conversely, no significant differences in term of mean R.E.N.A.L. score or CCI were found among the two groups [19].

5.4 Role and Modalities of Active Surveillance of Small Renal Tumours

Surgical removal is the treatment of choice for SRMs. Nephron-sparing surgery is currently the gold standard for these lesions, since it was shown to achieve similar oncological outcomes of radical nephrectomy with less impact on renal function [20–22]. Overall, the outcomes of surgery for <4 cm (pT1a) RCCs are excellent. In an international multicentre study including 1454

patients, Patard et al. observed a cancer-specific survival at 5 years close to 97% after nephron-sparing surgery [23].

Surgical complications of nephrectomy have decreased with the improvement of surgical techniques but are still significant especially in the elderly population [24]. This is clinically important since an increasing number of incidental renal tumours are diagnosed in elderly patients who undergo radiological examinations for other medical problems. These patients often have significant comorbidities and therefore a higher risk of postoperative morbidity and mortality.

Despite the increased incidence of low-grade neoplasms and the excellent results of surgical treatment of SRMs, mortality from RCC has not decreased in recent years [25]. This suggests a potential overtreatment of a proportion of small renal tumours with a long natural history and a limited risk of progression. This concept is also supported by autopsy studies. Hellsten et al. showed that 67–74% of RCCs used to remain unnoticed until death before the diffusion of modern imaging techniques. Moreover, only 9–20% of all diagnosed RCCs were in fact responsible for the patient's death [26].

Based on these observations and on the analysis of data that are gradually emerging about the natural history of SRMs, it is necessary to review the indications of immediate surgery for all small renal tumours. In fact, many incidentally discovered SRMs are not histologically malignant or have an indolent clinical behaviour and therefore do not represent an immediate threat to the patient's life. This is especially true for elderly patients or patients with significant comorbidities.

In fact, non-RCC-related mortality after surgical treatment for SRMs is significant and correlates with age and the presence of other medical conditions. A population-based analysis of 26,618 patients who were surgically treated for loco-regional kidney cancer between 1983 and 2002 showed that about 40% of patients who are >70 years old and have a kidney tumour <4 cm died from unrelated causes in the 5 years following the surgical removal of their tumour [27]. In a retrospective review of 192 patients with clear cell RCC, Arrontes et al., observed that a CCI >2 was significantly associated with a worse overall survival after surgical treatment ($p < 0.001$) [28].

Finally, an interesting study from the Cleveland Clinic reported the oncological outcomes of a series of 537 patients with <4 cm renal tumours who were either surgically treated or followed with active surveillance. Only age and comorbidities were found to be independent predictors of overall survival in this series, while surgical removal did not provide any significant survival advantage [29]. No statistically significant differences in overall and cancer-specific survival were observed in another study of radical nephrectomy vs. partial nephrectomy vs. active surveillance for T1a renal masses with a follow-up of 34 months [30].

Population-based studies also compared the oncological outcomes of surgical and non-surgical management for tumours <4 cm. The analyses showed a significantly lower cancer-specific mortality for patients treated with surgery [31, 32]. However, the patients assigned to the surveillance arm were older and likely to be more frail and less suitable candidates for surgery. Other cause mortality rates in the non-surgical group significantly exceeded that of the surgical group [31]. Population-based analyses in older patient populations (>75 years) failed to show the same benefit in cancer-specific mortality for surgical treatment [33].

Therefore, a limited life expectancy and the presence of concomitant medical comorbidities may significantly reduce the survival advantage provided by surgical extirpation of renal tumours [34]. An estimate of the risk of competing cause mortality can be useful in order to decide the most appropriate treatment for patients with renal cancer. This can be easily obtained with the use of specific nomograms [35, 36]. In patients with SRMs who are elderly or have significant comorbidities, and life expectancy is less than the time the cancer will take to progress, active surveillance can be proposed as a reasonable option [37].

The concept of active surveillance implies an initial period of observation of the growth rate and clinical behaviour of a SRM with serial abdominal imaging, with a delayed active treat-

ment reserved only for those tumours which show a fast growth or clinical progression [8]. It has been observed that tumours that will eventually metastasize have a significantly greater growth rate during surveillance compared to those that will not [10, 38]. No standardized criteria for delayed intervention during active surveillance have been yet defined. However, a diameter of 3–4 cm or a tumour volume doubling time <12 months under surveillance is generally used to identify renal masses at greatest risk of progression which should prompt active treatment. Further studies are needed to define precise and evidence-based criteria to indicate delayed intervention. With a careful use of surgical treatment for tumours with fast growth, the risk of progression to metastatic disease during surveillance appears very limited. Crispen et al. analysed the outcomes of 87 patients treated with delayed intervention after active surveillance for a median period of 14 months (>24 months in 33% of cases) at the Fox Chase Cancer Centre, Philadelphia, USA. In this series, delayed treatment was not shown to preclude or complicate active treatment, including nephron-sparing surgery or minimally invasive surgical approaches. Tumour progression to pT3a disease was observed only in one case, and there were no cases of metastatic progression [39].

The optimal follow-up schedule for patients on active surveillance has yet to be defined. It is generally recommended to perform a triple phase abdominal scan every 3 months in the first year, then every 6 months up to 3 years, and every year thereafter in cases of little or no growth of the SRM [8]. Computed tomography (CT) scans may sometimes be replaced by ultrasound—possibly with contrast enhancement—when there is dimensional stability and good visibility of the renal mass on ultrasound. This approach can decrease radiation exposure for the patient and treatment costs. Chest imaging should be also performed every 6 months in the first 3 years and annually thereafter to exclude metastatic progression to the lungs.

When the patient's clinical conditions contraindicate a delayed treatment, the follow-up schedule should be less intensive, and imaging should be mainly performed in the presence of signs of symptoms indicating clinical progression.

Overall, active surveillance requires an adequate and thorough patient counselling, a precise organization of follow-up and a good patient compliance.

All published series of active surveillance include a large proportion of patients with unknown tumour histology. This represents a bias in the interpretation of the oncological outcomes. Results from multicentre studies with long follow-up and histological confirmation of the disease with a percutaneous biopsy at diagnosis are needed to confirm the safety of active surveillance in the management of patients with histologically confirmed RCC. In the absence of a curative treatment for metastatic disease, this conservative approach should not be recommended for young patients with low surgical risk outside clinical studies. Active surveillance for larger T1b tumours should also be considered only for highly selected and well-informed patients, since the promising outcomes reported to date must be carefully interpreted, mainly because of the relatively short follow-up. Finally, information on histology and biological aggressiveness obtained with renal tumour biopsy (RTB) can have a very important role in treatment decision-making for SRMs and in particular for the selection of patients to include in active surveillance protocols.

5.5 The Role of Percutaneous Biopsy in the Management of Small Renal Masses

Percutaneous biopsy of renal neoplasms has historically been used for only limited indications, including the differential diagnosis of lymphoma, the diagnosis of renal metastatic disease in the presence of a known extrarenal malignancy and the histological characterization of surgically unresectable retroperitoneal tumours or of primary renal tumours in the setting of diffuse metastatic disease.

Beyond these clinical scenarios, biopsies of renal tumours have been rarely used given

uncertainty over their safety (perceived risk of tumour seeding along the needle tract and haemorrhagic complications), diagnostic rate and accuracy and their effectiveness in terms of impact on clinical decisions, due to the perception that all solid renal masses have a malignant potential and should be removed surgically. Many of these uncertainties have now been overcome due to the growing experience of urologists and interventional radiologists in performing biopsies, the growing experience of pathologists in interpreting specimens and the growing confidence of urologists to use information from biopsies to support clinical decisions.

From a practical standpoint, RTBs are generally performed on an outpatient basis under local anaesthesia and are generally well tolerated. Biopsies can be performed under ultrasound, CT or MRI guidance according to physician's preference, tumour location and size and patient's habitus. When possible, an ultrasound guidance is preferred, since it allows a puncture in real time, does not expose the patient to any radiation exposure and has low costs. However, CT guidance should be preferred in obese patients and for masses with poor ultrasound visibility and is more frequently used for renal masses located in the upper pole, at the anterior margin of the kidney or with a size <15 mm.

RTBs are generally performed with 18G Trucut needles. The use of full-core needles appears to provide better results both in terms of diagnostic yield and diagnostic accuracy. Smaller needles (≤21 G) are used for fine needle aspiration (FNA). However, a recent systematic review and meta-analysis have shown the superiority of core biopsies over FNA for the histological characterization of renal tumours [40]. The "coaxial" technique is mandatory to reduce the risk of dissemination along the needle tract. A guiding cannula is placed just inside the tumour. The stylet is then removed, and the biopsies are taken with an automatic biopsy gun through the guiding cannula. Multiple samples can be obtained through the cannula that is left in place and finely repositioned within the lesion to allow sampling of different areas without being extracted.

At least two good quality samples should be obtained in different regions of the tumour, avoiding areas of necrosis. Wunderlich et al. observed a lower diagnostic accuracy for central biopsies in tumours >4 cm, likely because of the more frequent presence of necrosis in the central portion of large renal tumours [41]. Based on these results, it is recommended to obtain a central and a peripheral biopsy in tumours <4 cm and two peripheral samples in tumours >4 cm.

Complications of RTBs are uncommon with the use of modern biopsy techniques and mainly comprise immediate or delayed bleeding, since kidney tumours are generally hypervascular. However, bleedings that require hospitalization and/or blood transfusion are rare in experienced centres (<1%) [42]. The risk of tumour seeding along the needle tract is anecdotal, with very few cases reported with the use of modern biopsy techniques [43].

In recent series from centres with experience, needle biopsy of solid renal tumours has a good detection rate (78–97%) and high specificity (98–100%) and sensitivity (86–100%) for the diagnosis of malignancy [42] (Table 5.3). A recent meta-analysis of 33 studies on RTBs with lower risk of bias has shown an overall diagnostic rate of 92% and a sensitivity and specificity of core biopsies for the diagnosis of malignancy of 99.1% and 99.7%, respectively [44]. The diagnostic accuracy of RTBs for the diagnosis of tumour histotype is also high (90.3% overall and 96% for SRMs in the reported systematic review and meta-analysis) [46]. Conversely, the accuracy for the assessment of Fuhrman grade (I–IV) is only fair (43–75%) but can be increased using a simplified grading system (high grade vs. low grade) [42, 46].

RTBs have lower diagnostic rates for cystic renal masses and should not be generally recommended for these lesions, except for Bosniak IV masses [45]. The combination of core biopsy and FNA can obtain complementary results in these patients [47].

The increased incidence of SRMs and the availability of alternative treatment options for these lesions in selected patients increased the awareness that pretreatment characterization of

Table 5.3 Diagnostic performance of renal tumour biopsies of renal tumours in the largest available series

	No.	Mean tumour size (cm)	Guidance	Needle size (G)	% diagnostic biopsies	Accuracy for malignancy	Accuracy for histotype (%)	Accuracy for grading (%)
Neuzillet et al., J Urol (2004)	88	2.8	CT	18	91	92%	92	69.8
Shannon et al., J Urol (2008)	235	2.9	CT/US	18	78	100%	98	NA
Schmidbauer et al., Eur Urol (2008)	78	4.0	CT	18	97	Sensitivity 93.5% Specificity 100%	91	76
Lebret et al., J Urol (2007)	119	3.3	CT/US	18	79	86%	86	46/74
Maturen et al. AJR (2007)	152	4.1	CT/US	18	96	Sensitivity 97.7% Specificity 100%	NR	NA
Volpe et al., J Urol (2008)	100	2.4	CT/US	18	84	100%	100	66.7/75
Wang et al., Urology (2009)	110	2.7	CT/US	18	90.9	100%	96.6	NA
Veltri et al., Eur Radiol (2011)	103	3.4	US	18	100	NR	93.2	NA
Leveridge et al., Eur Urol (2011)	345	2.5	CT/US	18	80.6	99.7%	88	63.5

NA not available

renal tumour histology is necessary to tailor the best-suited treatment to each individual patient, with a significant impact on clinical practice [42].

Pretreatment percutaneous biopsy can indeed reduce the number of unnecessary surgical indications for patients with benign renal tumours, especially in the elderly population with comorbidities. As previously mentioned, SRMs are in fact benign in a non-negligible proportion of cases, with a probability that significantly increases with decreasing tumour size [48–50]. Conventional radiology (CT scan, multiparametric MRI, contrast-enhanced ultrasound) does not allow a reliable diagnosis of oncocytoma. The typical appearance of this benign tumour as a homogeneous, hypervascular mass with a starry central scar is actually observed in a limited number of cases. Moreover, no other radiological CT or MR feature is sufficiently accurate for the diagnosis of this benign tumour [51, 52]. In addition, although most angiomyolipomas are easily diagnosed at CT for their characteristic fatty content, low-fat angiomyolipomas (leiomyoma-like and epithelioid variants) cannot be properly diagnosed by radiological investigations [53]. Overall, Remzi et al. observed that only 17% of benign tumours are correctly identified by preoperative CT scan [54].

Furthermore, percutaneous biopsy can support for choice of the best-suited treatment for all localized renal tumours, especially in patients with limited life expectancy and high surgical risk. Biopsy is particularly useful to select patients who are eligible for a conservative treatment. In fact, active surveillance is a reasonable option for tumours with low-grade histology and therefore limited risk of progression, while surgery should be always advocated—whenever possible—for tumours with aggressive histology. Information from RTBs can also be of help to plan the intensity of follow-up in patients in active surveillance. In fact, benign tumours at biopsy can be followed with a less stringent follow-up schedule, thereby reducing the risks of

radiation exposure and the costs for the healthcare system.

Percutaneous biopsy may also be performed in selected cases of larger renal tumours (T1b-T2). In fact, although the decision to perform a radical or partial nephrectomy depends essentially on patient's characteristics and on tumour features at imaging, biopsy may favour the choice of radical nephrectomy for aggressive disease at pathology and conversely support the indication of nephron-sparing surgery in cases with high anatomical complexity in the presence of benign disease or tumours with indolent biological potential. In summary, percutaneous RTBs can provide important information for treatment decisions in patients with SRMs. Research studies are needed to determine the ideal pattern of biopsy (number and location of cores according to tumour size) in order to optimize the diagnostic results. The application of cytogenetics and molecular markers on biopsy specimens has the potential to provide further diagnostic and prognostic information, thereby further increasing the role of percutaneous biopsy in the management of renal neoplasms.

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Image-Guided Radiofrequency Ablation for Small Renal Masses

6

Emily F. Kelly and Raymond J. Leveillee

Abbreviations

CA	Cryoablation
EMN	Electromagnetic navigation
MWA	Microwave ablation
NSS	Nephron-sparing surgery
PN	Partial nephrectomy
RCC	Renal cell carcinoma
RFA	Radiofrequency ablation
RN	Radical nephrectomy
SRM	Small renal masses
TA	Thermal ablation

Key Messages

- As provider experience improves and long-term outcome studies become available, thermal ablation is becoming increasingly accepted as a potential new standard of care for solid small renal masses.
- Radiofrequency ablation (RFA) can be delivered using various percutaneous image-guided or laparoscopic techniques.
- The mechanism of action of RFA depends on the principle of heat conduction inducing cellular death.
- Emerging data show that long-term efficacy of radiofrequency ablation for managing small renal masses is approaching that of partial nephrectomy.
- Radiofrequency ablation offers fewer complications, faster convalescence, shorter hospital time and an option for patients who cannot undergo general anaesthesia.

6.1 Introduction

The diagnosis of incidental small renal masses (SRM), most commonly renal cell carcinoma (RCC), has increased during the past two decades due to the increased availability and utilization of

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imaging [1, 2]. Since 1970, the incidence of RCC has increased 3 and 4% per year in the Caucasian and African-American populations, respectively. SRM encompass clinical stage cT1a <4 cm [3]. In recent years, the standard treatment of SRM has shifted from radical nephrectomy (RN) to nephron-sparing surgery (NSS) in which partial nephrectomy (PN) has become the new standard of care for tumours which do not invade the collecting system [4]. The goal of NSS is to resect/ablate the tumour and small surrounding rim of healthy tissue to ensure negative margins while preserving an optimal amount of renal function, i.e. "collateral damage" [4, 5]. While allowing for the preservation of normal renal parenchyma, NSS is associated with improved long-term outcomes. NSS options include PN, thermal ablation (TA) and nonthermal ablation (irreversible electroporation) where cryoablation (CA), microwave ablation (MWA) and radiofrequency ablation (RFA) are the most common forms of TA [5]. The decision between procedures is based on the experience of the team, urologist and interventional radiologist and access to equipment. It is beyond the scope of this review to discuss in detail these alternative options; thus, we will primarily focus on RFA.

6.2 Management Guidelines for RFA

Currently the literature suggests that RFA is most successful in SRM <4 cm. In 2009, the American Urological Association (AUA) published clinical guidelines for treatment of SRM. TA was suggested as a treatment option in patients with T1a tumours and major co-morbidities and/or patients unable to undergo surgery. This includes patients of increased age, renal insufficiency, bilateral tumours and local reoccurrence and patients with VHL syndrome. Additionally, the update suggested TA as an option in healthy patients with T1a/b lesions, as well as patients with major co-morbidities with stage T1b tumours [6, 7]. Furthermore, the European Association of Urology recommends TA not only for patients with major co-morbidities but for healthy patients with SRM. Although PN remains the standard of care, this treatment modality is associated with increased warm ischemic time and increased risk of urologic complications including haemorrhage and urinary fistula formation. Compared to PN, TA offers fewer complications, faster convalescence, shorter hospital time and an option for patients who cannot undergo general anaesthesia.

6.3 Support/Results

Gervais et al. report a retrospective series of 100 renal tumours treated with RFA. One hundred percent of SRM <3 cm, 92% of 3–5 cm masses and 25% of masses >5 cm were treated successfully [1, 2]. Zagoria et al. demonstrate that with each 1 cm increase in diameter above 3.6 cm, the likelihood of recurrence-free survival decreases by a factor of 2.19 and recommends caution when treating tumours >4 cm [8]. Olweny et al. compare the 5-year outcomes for RFA vs. PN in T1a-treated RCC and report 97.2% vs. 100% (p = 0.31) cancer-specific survival, 97.2% vs. 100% (p = 0.31) overall survival and 91.7 vs. 94.6% (p = 0.96) local recurrence-free survival [9]. Psutka et al. report on 185 patients with T1 RCC followed for a mean of 6.43 years. The overall disease-free survival rate was 88.6% (92.3% T1a and 76.3% for T1b), and only 13% of patients were retreated for recurrence [10]. Please refer to Table 6.1 for additional results.

6.4 Principles of Radiofrequency Ablation

6.4.1 Mechanism of Action

RFA, a form of hyperthermal ablation, was originally developed for the treatment of aberrant cardiac pathways and now is used for renal masses and prostate hyperplasia. The main mechanism of RFA depends primarily on the principle of heat conduction inducing cellular death [4]. Secondary mechanisms include vaporization and coagulative necrosis. Alternating current with a

Table 6.1 Long-term outcomes following RFA for SRM

	Ma et al. [33]	Lorber et al. [13]	Kim et al. [34]	Zagoria et al. [8]	Tracy et al. [35]	Balageas et al. [36]	Ramirez et al. [37]
Pt number	52	50	47	41	208	62	79
Tumour number	58	53	48	48	243	71	111
Tumour size	2.2	2.3 (0.3–4.0)	2.3 (1.0–3.0)	2.6 (0.7–8.2)	2.4	2.3	2.2 (0.9–4.2)
Approach: lap	24	24	12	0	68	0	111
percutaneous	34	29	36	48	172	71	0
Long-term F/U (months)	60.1 (48–90)	65.6 (48.5–120.2)	49.6	56 (36–64)	27 (1.5–90)	38.8 (18–78)	59 (2–120)
Incomplete ablation	0%	0%	10.4% ($n = 5$)	NA	2.9% ($n = 7$)	4.8% ($n = 3$)	2.5% ($n = 2$)
Local reoccurrence	5.1%	7.5%	8.3%	12% ($n = 5$), (0% <4 cm)	3.7% ($n = 9$)	12.7% ($n = 9$)	6.3% ($n = 5$)
Recurrence-free survival	94.2%	92.5	NA	88%	93%	NA	93.3%
Disease-free survival (5 years)	NA	90.6%	NA	83%	NA	61.9%	NA
Overall	95.7%	98%	NA	66%	93%	82.3%	72%
survival – 5 years/10 years	91.1%	93%	NA	NA	Na	60.9%	NA
Cancer-specific survival	100%	100%	NA	NA	99%	96.8%	100%
Metastasis	0%	1.9%	0%	7% ($n = 3$)	1.2%	6.5%	0%
Probe type	14-G starburst XL	Cool-tip (90%) StarBurst RITA (10%)	Cool-tip	Cool-tip	StarBurst XL	LeVeen	Starburst XL

frequency between 375 and 900 KHz is delivered by a generator to an electrode probe which has been placed in the centre of the target tissue. Most often these systems are monopolar thus requiring a single grounding pad. The ablation zone of thermal conductivity remains unmodified 1–2 mm from the tip of the needle probe [11]. The resulting coagulation provides an advantage of RFA since no topical haemostatic agents are required post-ablation to control bleeding as has been seen with CA [4]. The effects of RFA-induced cellular injury rely on a time-temperature curve where ablations at higher temperatures require less time. Bhowmick et al. describe this phenomenon demonstrating that irreversible cellular damage occurs after 60 min at 45 °C, 5 min at 55 °C or 1 min at 70 °C [5]. As temperature increases, ionic agitation of intracellular molecules develops resulting in frictional heating. Once temperatures reach above 60 °C, the cell loses its intracellular buffering capacity which results in the accumulation of intracellular calcium and eventual cellular death. As local inflammation increases, acidosis occurs and coagulative necrosis results [1, 2]. As the temperature increases, different phases of cellular damage are observed. Coagulation and cellular damage, secondary to protein denaturation, blood coagulation and irreversible cellular death, result after exposure to temperatures between 50 and 80 °C for seconds to minutes. Vaporization damage resulting in dehydration, vacuole formation and tissue ablation occurs at temperatures above 100 °C. Lastly, carbonization in the form of melting and charring transpires once temperatures reach between 150 and 300 °C [4]. Carbonization

is to be avoided as a zone of extremely high impedance results, thus limiting RF current passage and thermal spread.

The success of RFA depends on a temperature-based algorithm and treatment endpoints detected by temperature monitors, temperature probes and impedance probes [12]. We recommend that a temperature goal of at least 60 °C be obtained in order to achieve instantaneous irreversible cell damage by denaturation of proteins and coagulative necrosis (Fig. 6.1). General, conscious and intravenous sedation are anaesthetic options for RFA procedures; general anaesthesia is ideal. Under general anaesthesia, the respiratory cycle can be manipulated allowing for more accurate probe placement [1, 5].

6.4.2 Effect of Tumour Size and Location

Tumour size and location are strong predictors of ablative success [13, 14]. Heat loss is directly dependent on the average blood flow within a tissue. Therefore, when flow rates increase, "heat sinking" occurs and is responsible for the observed increased rate of incomplete ablations of vascular tumours, secondary to the location of proximal vessels [4, 5, 11]. Limitations of RFA are determination of end treatment, probe placement during different stages of the respiratory cycle and accumulation of error which is seen between steps. End treatment goal is debated since heat cannot be visualized by CT or US. It has been demonstrated, however, that real-time temperature monitoring through non-conducting fibre optic probes allows for the establishment of adequate treatment endpoints and expands the size and location of tumours treated [4, 12, 13, 15, 16].

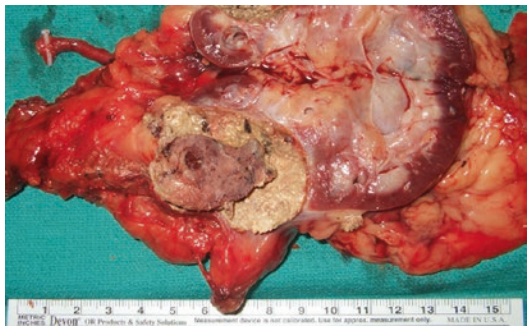

Fig. 6.1 Gross image (confirmed histologically) demonstrating complete destruction of 4.7 cm left renal clear cell carcinoma via coagulative necrosis. The kidney removed at 12 months follow-up after being treated successfully by laparoscopic RFA, Cool-tip® (Valley Lab, Boulder, CO, USA) under laparoscopic US image guidance

6.4.3 Advances: Real-Time Temperature Monitoring

Determination of the endpoint of treatment can be achieved with real-time temperature monitoring using fibre optic temperature probe(s) (Luxtron Corp., Santa Clara, CA). The use of these probes which are non-conductive allows for the determination of the precise temperature of the ablation zone in real time. Determination of end treatment when all probes reach at least 60 °C at the tumour periphery decreases the number of incomplete ablations and improves precision [5, 12, 13, 16].

6.4.4 Not All RF Probes Are the Same

The mechanism of action whereby RF generates temperatures is via metal electrode/tissue interactions. Alternating electromagnetic (AC) waves (between 10 kHz and 900 MHz) pass through tissues and result in ionic agitation with subsequent heat generation. At the probe/tissue interface, a significantly high proportion of current density occurs creating potentially extremely high local temperatures with resulting carbonization which ultimately inhibits heat conduction. The goal is to heat at lower sustained temperatures and not cause carbonization (avoid "charcoaling"). Several engineering designs have been employed to try to obviate this high current density – these include expanding the surface area with deployable needles, LeVeen® RF system 3000® (Boston Scientific, Natick, MA, USA) and RITA StarBurst® (Angiodynamic®, Queensbury, NY, USA), as well as internal cooling to prevent tissue desiccation at the metal/tissue contact point,

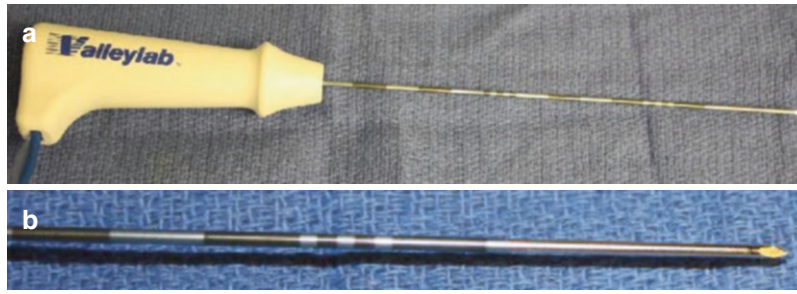

Fig. 6.2 (**a**) The straight needle, Cool-tip® (Covidien, Valley Lab, Boulder, CO, USA) probe with hand piece. Circulation of chilled water into the hollow channel of the needle prevents overheating and charring allowing for wider dissemination of electrical current. (**b**) Close up of Cool-tip® demonstrating uninsulated active tip (*bracket*) and centimetre calibrations proximally

Fig. 6.3 The multilined, expandable RITA StarBurst® (Angiodynamic®, Queensbury, NY, NY, USA) electrode. Adjustable tine spacing allows for single needle placement creating a predictable expansion of the tines. Extreme expansion may create nonspherical lesions due to conductive heat loss

Cool-tip® (Covidien, Boulder, CO, USA). This allows electrical current to emanate away from the metal antenna and still create heat several mm away from the needle probe. Saline tissue perfusion (Talon ™, Angiodynamic®, Queensbury, NY, USA) will spread current density away from the metal tip and increase the ablation target zone (Figs. 6.2 and 6.3) [2, 5]. It is beyond the scope of this manuscript to describe in great detail the pros and cons of each design; however, we feel it is important for the reader to be cognizant of the fact that not all RFA probes work the same. This may impact interpretation of results seen in Table 6.1.

6.4.5 Contraindications

RFA is contraindicated in patients who have a life expectancy of less than 1 year, multiple sites of metastasis at the time of procedure, the presence of an irreversible haematological coagulopathy and/or result of respiratory complications when in the prone or supine position for the length of the procedure.

6.5 Percutaneous Radiofrequency Ablation

Percutaneous RFA is utilized for most tumours but is optimally suited for laterally and posteriorly located renal masses away from vital intraperitoneal organs. In contrast, the laparoscopic approach allows for the manipulation of the surrounding anatomy in anteriorly located tumours, limiting thermal damage [4]. Imaging is often utilized for laparoscopic RFA; however, presently this is limited to ultrasound for probe placement. We will focus our discussion on percutaneous needle placement; imaging techniques include conventional

computerized tomography (CT); CT fluoroscopy; magnetic resonance imaging (MRI), possibly augmented by three-dimensional renderings; and image fusion techniques [1, 4]. Of these techniques, CT-guided RFA is most commonly utilized [5, 17].

6.5.1 CT-RFA

CT-RFA can be achieved in either the prone or lateral decubitus position allowing for access to posteriorly or laterally located tumours. The authors recommend that CT-RFA be performed under general anaesthesia allowing for accurate probe placement under the guidance of a CT grid [1, 4, 11]. This prevents patient movement and helps regulate the breathing cycle – thus improving accuracy. After the initial skin incision is made, a 16 gauge biopsy cannula is guided by means of intermittent CT imaging. Once the position is confirmed, the stylet is withdrawn. Next, via the cannula, fine needle aspiration can be performed (optional) with a 22 gauge Chiba needle. Alternatively (authors' preference) core needle biopsies are obtained, through an 18 gauge spring-loaded biopsy needle [1, 4]. A minimum of three cores are encouraged. At this time, the TA probe is placed in the same trajectory as the biopsy needle but *not* through the metal biopsy guide as this will increase the risk of capacitive currents and collateral damage, especially skin burns. Once the TA probe is radiographically confirmed to be in proper position, ablation is performed according to manufacturer's specifications and clinician's judgement (Fig. 6.4). Ablation of the access tract is recommended to ensure cellular death and to aid in haemostasis. Post-ablation the probe is withdrawn and a small adhesive bandage is applied. Local anaesthetic (lidocaine 1% or Marcaine 0.25%) can be utilized at the puncture site but is optional. It is reasonable to perform an end of procedure CT image to document any perirenal fluid collections such as haematoma or urinoma. If intercostal access is utilized, a post-procedural chest radiograph is recommended to rule out thoracic complications such as pneumothorax or haemothorax. Follow-up imaging is performed typically at 6 weeks, 6 months and annually for up to 5 years [1, 4, 11, 32].

CT-RFA has several advantages in comparison to the laparoscopic approach. First, access to CT scanners is ubiquitous [17]. Next, the length of hospital stay is decreased, since patients can receive ablation at outpatient facilities which further decreases the cost of the procedure. Furthermore, complications of insufflation and laparoscopic manipulation of vital organs are avoided resulting in fewer post-procedural complications [4]. Limitations of this approach include diameter of gantry opening, patient size, time required for needle repositioning, patient exposure to radiation and contrast material and inability of real-time monitoring [11, 17].

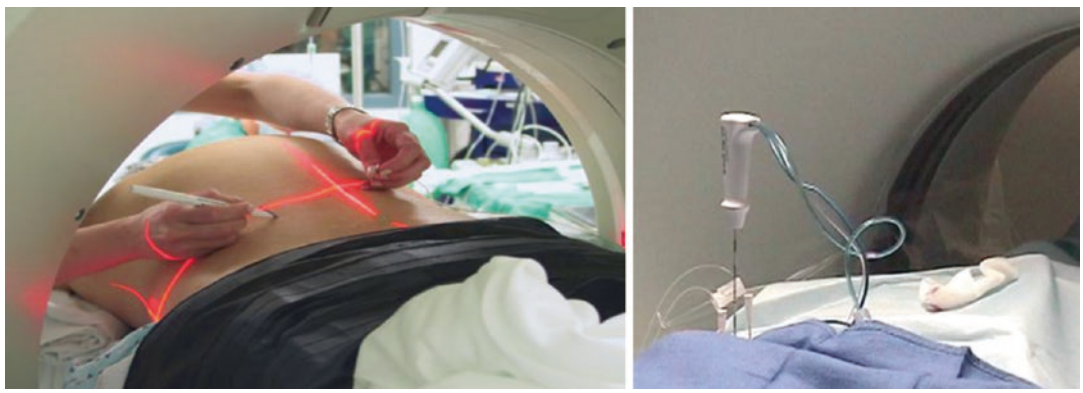

Fig. 6.4 (**a**) Patient, under general anaesthesia, placed on standard CT gantry. Laser cross-hairs projected to guide fingertip control of needle placement. (**b**) Post hand-assisted RFA probe placement

6.5.2 MRI-RFA

Although MRI-compatible RFA machines are not standard in interventional radiology suites, MRI-guided RFA provides several advantages when compared to CT-guided techniques. MRI-RFA was first described by Anzai et al. in 1995 for the treatment of brain tumours. Later Gervais and Mayo-Smith et al. have reported successful MRI-RFA for renal tumours. RFA is best performed with open-magnet MRI machines, for which two systems are available. The low-field biplanar scanner provides room for the provider to access the patient for probe employment. The high-field short-bore magnet design affords high temporal and spatial resolution however does not afford the physician as much room to access the patient for probe placement [2]. In order for RFA to be utilized under MRI guidance, MRI-compatible equipment is obligatory [4]. Two electrodes have been specifically developed for MR use. First, the nitinol StarBurst Semi-Flex® (Angiodynamic®, Queensbury, NY, NY, USA) electrode provides a more malleable shaft for triangulation and a larger ablation zone through the use of several dynamic tines [2]. The second, the titanium Cool-tip RF system® (Covidien, Boulder, CO, USA), provides maximum ablation size while simultaneously cooling with circulating water [2, 4]. Lewin et al. describe effective MRI-RFA treatment delivered through the Cool-tip RF system® for 12–15 min at 90 °C guided via real-time temperature probes [4].

Axial-fast spin-echo imaging allows for the planning of probe entry. The trajectory is then placed under continued MR guidance. Guidance can be aided by either the three-slice method or the triorthogonal image plane method. While centred on the probe shaft, the three-slice method utilizes three parallel 5 mm slices providing feedback of deviance from the focus of the middle slice of the preset trajectory allowing the provider to advance along the correct path. The triorthogonal image plane uses modifiable sagittal, coronal and axial scans which are taken in real time to form a single image which is then projected on the patient to guide the path of the probe along the trajectory [2]. Both the three-slice and triorthogonal image plane methods are tools to help improve probe placement accuracy.

High spatial resolution images allow for target confirmation. If the StarBurst Semi-Flex® electrode is utilized, an additional step must be completed to assure that the tines are evenly deployed and are at the level of the target and that the target has remained in the original position. Confirmation of tine placement is achieved via multiplanar imaging [2].

Ablation is then monitored via short tau inversion recovery (STIR) T2-weighted images. Successful ablations appear hypointense while enhanced lesions require repeat ablation. Once successful ablation is confirmed and probes are removed, post-ablation T1-weighted series are obtained to further ratify total tumour ablation, again by the absence of image enhancement [2]. Boss et al. reported that the repositioning of electrodes in tumours larger than 3.0 cm may be required to achieve complete ablation. Gervais et al. achieved successful MRI ablation in tumours as large as 5 cm [18]. Advantages of MRI-RFA include non-invasive real-time temperature assessment and elimination of ionizing radiation. Disadvantages of MRI-RFA include lengthier procedure time, incompatibility of ECG machines to monitor high-risk cardiac patients during the procedure, limited workspace of gantry, higher cost of machine and more limited availability, in comparison to CT. MRI-compatible RFA machines, unlike CT, may not be standard in all interventional radiology departments [1, 17].

6.5.3 Cone-Beam CT

Cone-beam CT-RFA uses a series of three-dimensional cross-sectional images to help guide the clinician along the predetermined trajectory path. Systems available include DynaCT (Artis Zeego, Siemens Medical Solutions, Erlangen, Germany), Innovact (GE Healthcare, Schenectady, NY) and XperCT (Phillips Healthcare, Amsterdam, Netherlands). Digital fluoroscopy coupled with these systems helps create a 3D reconstruction of the target tissue. Via the rotation

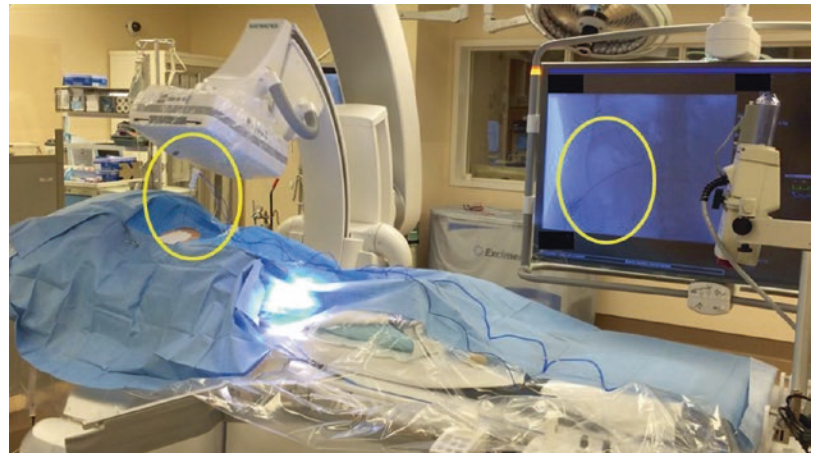

Fig. 6.5 Cone-beam CT room set-up. Notice the increased work space for probe placement. Screen highlights monitor used for fluoroscopic image guidance of needle placement (*yellow circles*)

of the large C-arm, hundreds of images from different angles can be taken via rotational fluoroscopy (Fig. 6.5*)*. These images can then be manipulated at the work station to create CT quality images. Additional software allows triplanar trajectory planning for probe/needle placement under fluoroscopic guidance. The entry point is then projected onto the patient via a cross-hair laser beam to guide the initial trajectory. Further needle manipulation is enhanced by preset fluoroscopic targeting paths (Fig. 6.6) [1]. Preliminary studies have shown comparable outcomes with shorter procedure times and decreased radiation exposure for patient and staff [19, 20].

Advantages of using this modality are increased work space for probe placement, increased biopsy and probe placement accuracy and decreased radiation exposure to the patient.

6.5.4 Electromagnetic Navigation

Electromagnetic navigation (EMN) combines and fuses pre-ablation CT scans with the EMN field to guide placement of the probe towards the target tissue in real time. The EMN field generator produces an alternate electromagnet field which utilizes positioned voltage producing RFA sensors located within small coils of the needle [1, 11, 21, 22]. The information from the sensors is then combined with passive fiducial markers placed on the patient's peripheral skin allowing for the real-time fusion of pre-ablation CT with the EMN system [1]. Systems which can be used include the Veran IG4 Plug-n-Play Delivery System (Veran Medical, St. Louis, Mo, USA) (Fig. 6.7) and the Aurora system (NDI, Waterloo, Ontario, Canada) [11]. Advantages of EMN include increased accuracy and decreased procedure time. However, the implication of this procedure can be expensive in obtaining the necessary hardware, coils and instruments [1].

6.5.5 Ultrasound CT Fusion

There are several different ultrasound CT fusion-based systems. Similar to the EMN system described above, US can be used in real time with the EMN system allowing for the fusion of pre-ablation CT, PET or US images. As in EMN, this system measures the voltage from the RFA needle coils; however, this information is then combined with in-procedure US to calculate needle position and angle selections for probe placement [1, 11, 21]. One system combining CT/PET images obtained pre-ablation with intraprocedural US was described by Venkatesan et al. using the PercuNav (Philips, Eindhoven, Netherlands). In combination with the already described EMN procedure, this system allows for PET/CT images to be fused on real-time US to guide the EMN tracked needle probes on the correct trajectory path towards the predetermined target. Post-confirmatory CT scans of needle probe placement showed a tracking error of

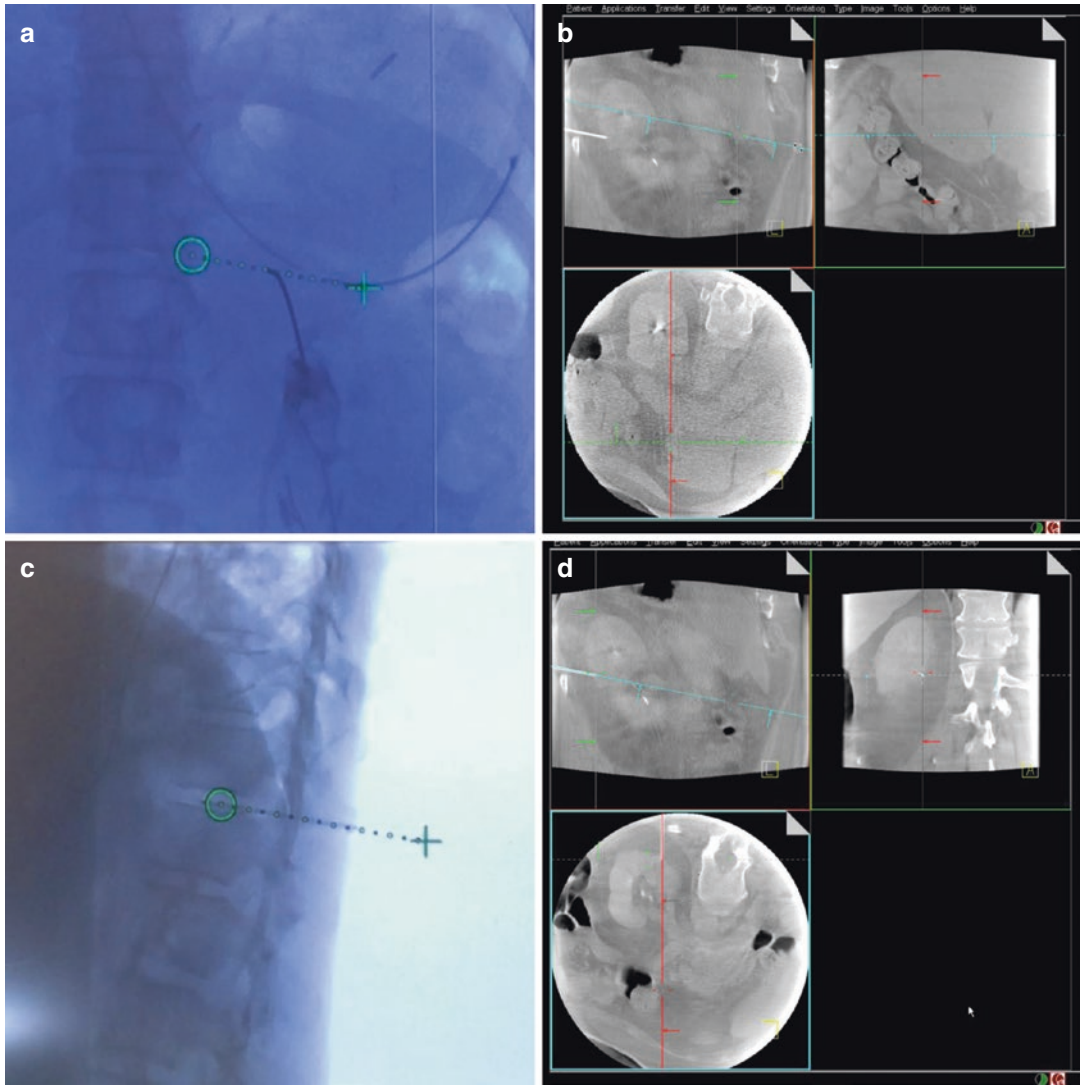

Fig. 6.6 Artis Q Zeego, Siemens, Germany, is utilized for probe placement. Movement of the C-arm aids in repositioning of the probe done under fluoroscopy. (**a**) Prior to fluoroscopic realignment, the trajectory, dotted line, is not aligned with the probe (*yellow arrow*) and placed in the kidney. (**b**) Axial, coronal and sagittal projections of target lesion. (**c**) iGuide software (Siemens) planning allows for needle advancement with fluoroscopic targeting. Once the final position is attained, it is confirmed with an additional "spin" (**d**) before biopsy and TA treatment

5.85 ± 4.48 mm without adding increased procedural time [1, 23]. Krucher et al. described a similar system using EMN position tracking sensor (Traxtal Inc., Toronto, Canada), renamed Traxtal PercuNav (Philips Healthcare, Andover, MD, USA) (Fig. 6.8), attached to the probe handle in 40 patients undergoing renal and liver ablations. The average tip to target error of all ablations was 3.8 ± 2.3 mm; liver-specific target error of 4.0 ± 1.9 and renal target error of 3.4 ± 2.1 were demonstrated [21].

Hung et al. reported another US/CT or US/MR fusion system used for the ablation of 32 virtual tumours in 16 canine kidneys. This system utilizes the Global Positioning System (MyLab 70 XVG, Biosound Esaote) which combines a virtual navigation system with 2D US. Advantages include the ability of US-obtained real-time two-

dimensional images to be superimposed onto pre-procedural-obtained CT or MR images. This permits real-time navigation of probe position. In this study, the average tip to target error was 1.8 mm. The virtual navigator aspect of the system predicts the amount of tissue ablated during the procedure allowing the provider to calculate the amount of remaining target tissue still requiring ablation. This reduces the need for subsequent ablation sessions. The accuracy of the procedural calculated ablation percentage was able to be determined after the animals were euthanized and gross specimen measurements were obtained. The performance results of the system were found to be significant (r = 0.5; P = 0.006) [24].

An advantage to the incorporation of US is real-time monitoring without exposure to radiation or contrast. However, there are many limitations. The quality of the image can become obstructed by bowel gas, RFA produced vaporization bubbles and large quantities of abdominal fat [25, 26].

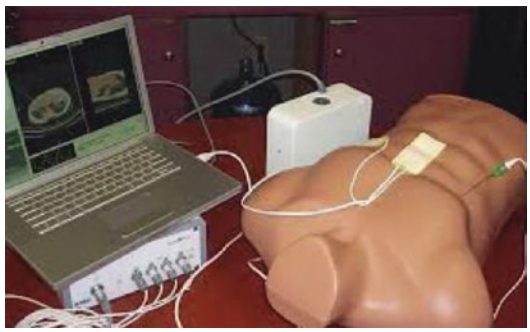

Fig. 6.7 Veran IG4 Plug-n-Play Delivery System (Veran Medical, St. Louis, Mo, USA) and EMN system

6.5.6 Camera Feedback

A camera-based system has been developed which can be used with inoperative CT to create a real-time three-dimensional CT image. Through the use of two calibrated cameras, the patient's respiration and movement can be tracked in real time allowing for precise placement of RFA probes. Target error has been reported as 2 mm in phantom and <5 mm in actual patients.

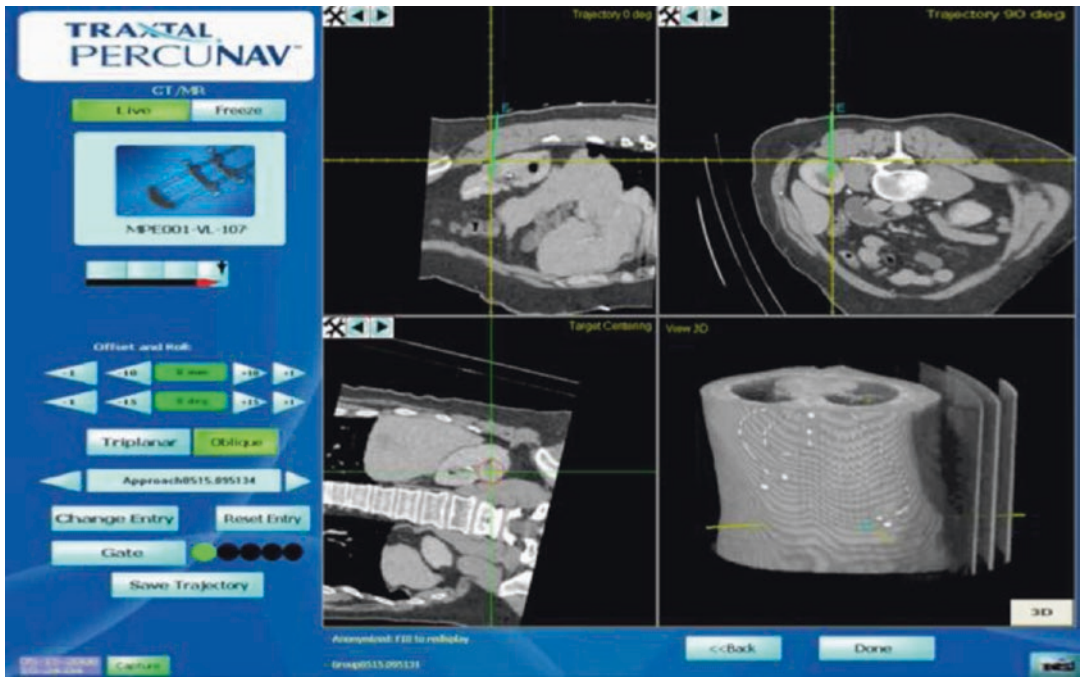

Fig. 6.8 Traxtal PercuNav (Philips Healthcare, Andover, MD, USA) ultrasound CT fusion-based system

6.5.7 Robot-Guided Ablation

This technique utilizes the CT-integrated robot (National Institutes of Health, Bethesda, MD, and Philips Medical Systems, Cleveland, OH) where the needle is placed mechanically along the trajectory [22].

Hong et al. further combined US/CT with a robotic needle holder. In this system, the alignment of the needle holder is robotically controlled allowing for compensation of respiration movement. The tip to target error reported in this system was 1.7 mm [1, 27]. Furthermore, with the use of a robot, radiation exposure to the urologist is eliminated when CT fluoroscopy is used. Other advantages of robotic needle placement include enhanced precision, accuracy and steadiness, when compared to human placement (Fig. 6.9). One challenge presented is in the mechanism of robotic movement which produces friction disrupting the insulation sheath of the probe. Solomon et al. are currently researching ways to improve this limitation. Other disadvantages include availability and increased set-up time [28].

6.5.8 Laser-Guided Ablation

This technology uses heat created by 700–1200 nm wavelength laser beam to achieve tumour ablation. CT, MRI or US can be used to direct the laser to the target tissue. A study conducted by Jacobi et al. utilized a laser-guided puncture support system (Partner-Diagnostica, Markt-Indersdorf, Germany). The advantage of this particular system is that it can be mounted on all "standard" CT machines. The use of the laser showed a deviation between 1.7 and 2.3 mm compared to 2.0 and 4.0 mm without the aid of the laser over the course of 160 punctures ($P < 0.5$). The improved accuracy was especially noted in unexperienced users. However, due to the lack of long-term studies, this modality has limited clinical use [5, 29].

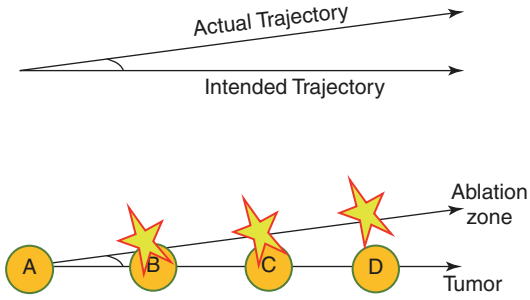

Fig. 6.9 Success in image-guided TA relies on precision. Even a misdirection of 1 or 2° can significantly impact targeting and efficacy

6.6 Laparoscopic RFA

Laparoscopic RFA is traditionally performed under US guidance for anterior tumours located within 2 cm of the bowel. The US image quality is limited by patient size, and the technique is difficult to master. Furthermore, US-guided needle placement is not as precise as CT-guided probe placement. Recently, laparoscopic DynaCT has been performed by Nozaki et al. for laparoscopic radical nephrectomy. This technique allows for the advanced ability to dissect and visualize the renal hilum while providing 3D planning allowing the surgeon to overcome limitations of conventional CT planning. This provides better operating room predictability and helps prevent unexpected surgical complications.

The authors of this chapter have recently performed the first known RFA ablation using laparoscopic thermal ablation (TA), in a hybrid operating room, using a fixed angiographic system (syngo DynaCT, Artis Q Zeego system, Siemens Healthcare GMbH, Forchheim, Germany). Patients who are not ideal candidates for partial nephrectomy are often offered with percutaneous CT-guided TA, as described above. In special circumstances, the tumour may be located too close to vital structures whereby collateral damage may occur. One option in these situations is instillation of isosmotic fluid to displace bowel (hydrodissection). Alternatively, laparoscopic exposure and simultaneous 3D imaging may be performed. The laparoscopic protocol is ideal for patients with anterior tumours located within 2 cm of the surrounding vital tissue (excluding the liver). This allows for the manipulation of vital structures while decreasing thermal injury to the spleen, bowel, ureter and other vital organs while further

reducing the number of post-procedural complications secondary to thermal injury. Coupling laparoscopic exposure with the DynaCT technology provides the advantage of enhanced precision of needle placement and decreased radiation exposure to the patient and staff as compared to conventional methods of targeting while avoiding damage to surrounding structures.

6.7 Complications of RFA

As with any invasive procedure, complications can occur and are usually decreased as technology improves and user experience increases. In general, TA offers significant safety as compared to other forms of NSS. Sterrett et al. described the results of a multi-institutional review for the long-term treatment outcomes of CA and RFA treatment of SRM compared to PN. The complication rate for PN was 13.7% compared to 8.3% for RFA [4]. Bleeding or post-ablation haemorrhage is the most common major complication observed in TA procedures. RFA which is haemostatic is associated with very infrequent bleeding complications. Haemorrhage is seen much more frequently as a complication of CA procedures when compared to RFA, especially for tumours >3 cm [30]. Ureteral or renal pelvic injury may also occur. TA if extended outside of the target tissue into the collecting system can result in urine leakage. Furthermore, ureteral injury secondary to stricture can result in hydronephrosis. Other complications include bowel injury, pneumothorax, tract seeding (risk <0.01%) and genitofemoral nerve injury, although less common. Injection of saline or 5% dextrose solution to displace the bowel is utilized by some interventional radiologists in order to increase spacing, thus limiting thermal injury. Unfortunately, this is not always successful technically [31].

6.8 Post-procedural Follow-Up

Success is defined by local recurrence and enhancement on imaging follow-up done by either MRI or CT imaging [5]. MRI serial images avoid the compounded effects of ionizing radiation over the post-ablation surveillance period. The ablation zone appears hypointense on T2-weighted and STIR images and hyperintense on T1-weighted images [2]. Follow-up by CT scan does subject the patient to ionizing radiation, and success is guided by <20 HU enhancement and no evidence of growth in the ablation zone [4]. Currently there is controversy in the literature about how often post-ablation surveillance should be conducted. Most investigators recommend follow-up images be performed 3, 6 and 12 months' post-ablation then yearly thereafter for up to 5 years [25]. The AUA Guidelines on imaging after NSS, specifically post PN, call for imaging annually for a minimum of 3 years, for low risk, and 5 years, for high risk [32].

6.9 Long-Term Follow-Up

Several studies have matured to demonstrate long-term efficacy very comparable to that of PN for SRM. Recently, Olweny et al. showed that the 5-year oncologic outcomes of RFA vs. PN in T1a-treated patients with RCC were similar, both having a cancer-specific survival rate greater than 95% [9]. However, PN still remains the standard of care secondary to the lack of studies demonstrating long-term outcomes of TA. With the improvement of provider experience and the increased availability of long-term outcome studies, TA is becoming more widely accepted as a potential alternative for the treatment of solid SRM.

6.10 Other Ablative Techniques

6.10.1 Cryotherapy

CA, a form of hypothermic TA, induces cellular death via the freeze-thaw cycle using the Joule-Thomson principle. Cellular freezing is achieved via probe-delivered pressurized argon gas resulting in cellular dehydration and membrane rupture when temperatures reach between -30 and -40 °C. Tissue damage results in the formation of an ice ball which can be visualized by ultrasound guidance. Subsequent reperfusion injury occurs in the thawing stage, induced by helium, causing microcirculatory failure and small vessel thrombosis.

6.10.2 Microwave Ablation

MWA achieves cellular death through frictional heating produced by electromagnetic waves. A wavelength frequency between 300 MHz and 300 GHz is required to generate tissue necrosis via the high-speed movement of water molecules within the ablation zone. The rotation of water molecules results in the absorption of heat leading to cellular death and ablation. An advantage of MWA is the ability to achieve successful ablations in tissues with previous thermal damage, low thermal conductivity and/or high impedance. A disadvantage of MWA is that the technique produces a larger ablation zone compared to RFA, thus limiting its clinical use in anteriorly located tumours.

6.10.3 Irreversible Electroporation

IRE, a nonthermal ablative technique, causes cellular death and apoptosis via a contained electrical force field produced between percutaneously placed probes. The high-voltage electrical current produced increases the permeability of the cell membrane, disrupts the electrochemical gradient and results in apoptosis. The end result of apoptosis is achieved when the amperage and voltage of 20–50 A and 1500–3000 V are attained. The main advantage of IRE is that apoptosis is not the product of thermal damage or coagulative necrosis. As a result, this tissue-sparing modality can be utilized for masses in close proximity to vital organs. Additionally, IRE allows for the ability to delineate the ablation zone while avoiding the heat-sink phenomenon. Since IRE is rarely performed for renal masses, there is limited data on its long-term effectiveness and follow-up.

Conclusion

Although PN is currently the standard of care for the management of SRM, image-guided TA through laparoscopic and percutaneous approaches is gaining support as technology expands and long-term studies are conducted. TA, in our opinion, is the future gold standard of SRM treatment protocols. Improvements in imaging modalities with ease of targeting to improve accuracy are being developed and perfected. With increased access, training and automation, TA will become a common practice. As more hospitals begin to integrate advanced imaging into "HYBRID" operating rooms, it is felt that possibly more surgeons will be performing these procedures as they broaden their armamentarium.

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Laparoscopic and Percutaneous Cryoablation of Small Renal Masses

7

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Abbreviations

AS	Active surveillance
BHD	Birt-Hogg-Dubé
CA	Cryoablation
LCA	Laparoscopic cryoablation
LESS	Laparo-endoscopic single-site
OR	Odds ratio
OS	Overall survival
PCA	Percutaneous cryoablation
PN	Partial nephrectomy
RCC	Renal cell carcinoma
RFA	Radiofrequency
RFS	Recurrence-free survival
RR	Relative risk
SRM	Small renal mass
TA	Thermal ablation
VHL	Von Hippel-Lindau

Key Messages

- Cryoablation is recommended by the EAU and AUA as an alternative treatment in high-risk surgical patients.
- Standard cryotherapy protocols consist of two freeze-thaw cycles with the resultant ice ball extending 5 mm beyond the tumour edge.
- Cryotherapy can be delivered using either a laparoscopic or percutaneous approach with the latter being increasingly favoured.
- Local recurrence is higher following cryotherapy compared to partial nephrectomy although a higher percentage of cryoablated patients have antecedents of previous RCC.
- While long-term data remains limited, recurrence-free survival rates are 80–100%, and cancer-specific survival rates are 89–100%.

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7.1 Introduction

The current EAU and AUA guidelines recommend ablation for cT1a renal tumours as an alternative treatment in high-risk surgical patients. Furthermore, AUA guidelines offer this option for cT1b tumours provided that the patient is properly informed on the greater risk of tumour persistence or recurrence. Wisely biopsy is now advocated in both guidelines prior to or during ablation [1, 2].

Since its inception in the 1990s, there has been a relatively steady increase in the number of ablations performed reaching a plateau of approximately 7% of all Stage I RCCs treated in the USA. Contemporary data from the CROES Renal Mass international registry, a predominantly European database, shows a slightly lower prevalence with ablation accounting for 3.5% of all interventional treatments in cT1 masses although in just cT1a masses this figure reaches 7% [3–6]. Cryoablation (CA) and radiofrequency (RFA) are the most frequently used technologies. Both can be delivered using laparoscopic or percutaneous approaches (US, CT or MRI guided). Historically RFA has been more frequently delivered by percutaneous approach, while laparoscopy was the preferred route for CA. However, the percutaneous approach has gained rapid acceptance and procedural percutaneous CA data is already extensively described in the literature [7, 8]. Open CA is limited to some initial reports and is not routinely offered [9].

In the last years, there has been a multitude of observational cohort studies, mostly retrospective, with small sample sizes and significant bias. In spite of these limitations, information on safety and short-term efficacy is available, and in the recent years, emerging data has offered the awaited long-term oncological outcomes, albeit with at the most level 2 evidence [10].

In this chapter, we will describe the case selection for CA of a small renal, the techniques of CA delivery either laparoscopic or percutaneous and the results in terms of complications and oncological outcomes.

7.1.1 Methods

No single RCT has compared the outcomes between ablation technologies, delivery techniques and with either nephron-sparing surgery or active surveillance. Consequently criteria for literature selection depend on the outcomes to be assessed. Although a systematic review may offer transparency and increased consistency, it will only offer a slightly higher level of evidence than the current literature. Meta-analysis, in spite of statistical corrections, is still likely to be biased by heterogeneity. For the purposes of outcome revision, a comprehensive review was performed including data on long-term outcomes previously compiled in a review [11] and adding most recent data from 2011 onwards. Only papers reporting more than 70 cases of CA, either percutaneous or laparoscopic, were selected for analysis of patient characteristics and peri-procedural complications. For oncological long-term follow-up, only papers focusing on RCC and with more than 36 months of mean/median follow-up were selected. In cases of successive reports of the same cohorts, the report with the largest follow-up was selected. Meta-analyses on CA as well as seminal papers were also considered.

7.2 Patient Selection

Selection of the appropriate candidates for CA requires a careful evaluation of the patient's general condition and tumour anatomical characteristics.

In most series, mean patient age varied between 62 and 73 years [12–14]. Patients treated with ablation are older and have a higher comorbidity load than those treated by partial nephrectomy (PN). However, there were no differences in age or tumour size between patients treated by ablation or active surveillance (AS) [15]. Comorbidities were more prevalent in patients treated by any form of thermal ablation (TA) than by excisional surgery [16]. A recent population-based analysis of over 5000 patients who underwent TA showed that 30%, 27% and 31% of the patients had 1, 2 or

≥3 comorbidities, respectively, and two or more comorbidities were present in 60% of those older than 50 years [17]. Furthermore, a number of studies of any TA technology exhibited a high percentage of patients with renal function impairment, with some cohorts showing a prevalence CKD ≥ 3 in up to 44% of cases [16–19]. The presence of "high-surgical risk" is a premise noted in the EAU guidelines as a selection criterion for TA [2]. However, the exact criteria for high-surgical risk remain unclear. ASA classification does not capture all details determining the complex perioperative interactions [20]. Comorbidity indexes are valuable in assessing survival and may even predict perioperative complications, but their predictive validity in assessing surgical risk remains uncertain. Nevertheless, while awaiting a definitive surgical risk classification, the current guideline statement includes young patients with cT1a renal masses who are considered "high-surgical risk" as candidates for renal mass ablation. Familial syndromes, Von Hippel-Lindau (VHL) and Birt-Hogg-Dubé (BHD), are also suitable for ablation [21].

The ideal tumour to ablate is a cT1a (maximal tumour diameter 4 cm). It has to be suspected to be malignant or enhancing in the contrast phases of CT scan or MRI. Mean tumour size varies in the literature from 1.9 to 2.7 cm with few series including tumours up to 7 cm [13, 22, 23]. All comparative series show that ablated tumours have a lower mean tumour size than those treated by NSS or AS [14, 15]. Table 7.1 displays the currently accepted indications for CA. When biopsied, RCC has been found in 55–79% of the ablated cases.

Table 7.1 Current indications for laparoscopic and percutaneous ablation

Indications for renal mass cryoablation
• cT1a tumour
• Elderly
• High comorbidity load
• CKD moderate or severe
• Solitary kidney
• Familiar RCC syndrome
• Patient's wish (*after informed discussion on recurrence risk if no other concomitant indication*)

Tumours treated by ablation are of lower complexity than those excised. When anatomical complexity scores are used, most of the tumours treated by ablation (91–97%) are classed as low or moderate R.E.N.A.L. nephrometry score [24–27]. The risk group distribution differs between different anatomical scores, but the higher prevalence of low- and intermediate-risk tumours remains unchanged when PADUA scoring is applied [26]. In the only series comparing R.E.N.A.L. nephrometry score between percutaneous CA and RFA, the CA group had higher scores than those treated with RFA (mean 7.2 vs. 6.1, $p < 0.001$) [25]. Some series suggest that CA may be preferred to RFA for those central and larger tumours even beyond the small renal mass (SRM) limit [28].

In a survey conducted by the AUA, patient's age, pre-existing comorbidity, tumour size and location were the most important factors to decide between the different excisional treatment options, ablation or surveillance in SRMs [29]. Similar results were shown in a Canadian survey [30]. Besides tumour and patient factors, utilisation of TA is higher in academic environment and increases with surgeons' volume [4, 31].

It is to be expected that patients will play an increasing role in treatment choice in SRMs. The subject has not been explored, but when faced, a thorough discussion should stress advantages and risks of ablation against PN or AS.

7.3 Technical Selection

Modern cryotherapy ablation is based on the Joule-Thomson effect, using argon to freeze and helium to thaw [32]. Two consecutive cycles of freezing and thawing are recommended to increase cellular damage and consequently the amount of tissue lethally treated [33]. Single (3.8–2.4 mm) or multiple ultrathin synergistic (1.47 mm or 17 gauge) probes are available with a clear trend in the last years in the use of the latter. The resultant *ice balls* provide a larger ablation zone that should engulf the renal mass and extend at least 5 mm beyond the external edges of the tumour. They may also minimise haemorrhagic

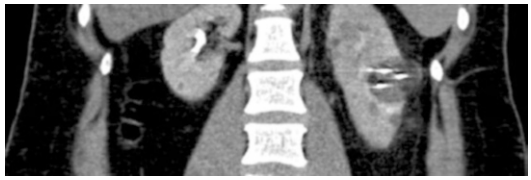

Fig. 7.1 Percutaneous ablation with a visible "ice ball"

complications by avoiding tearing and fracture of the tumour after thaw and probe retrieval.

Advantages of CA over RF include the real-time temperature monitoring, visibility of *ice balls* by imaging and modulation of the freezing rate to avoid tumour fissures (Fig. 7.1).

Renal CA is commonly performed by two minimally invasive routes, percutaneous (PCA) or laparoscopic (LCA), while laparo-endoscopic single-site (LESS) CA has been recently reported [34]. Population-based data from the USA (2006–2010) shows that overall laparoscopic TA is more frequently performed than percutaneous [17]. The first meta-analysis comparing CA to RFA showed that most CAs were performed with laparoscopic assistance [15]. No significant differences in patient age (median 67 vs. 66 years, $p = 0.55$) or tumour size (median 2.6 vs. 2.7 cm, $p = 0.24$) were found when comparing percutaneous to laparoscopic approaches [7]. However, a critical analysis on CA literature shows a clear shift favouring the percutaneous approach.

There are cases in which the percutaneous approach is lesser suitable. Laparoscopy is still indicated in anterior masses, when intestinal displacement manoeuvres are unsuccessful and when the mass is abutting the ureter and in upper pole masses that cannot be properly targeted with a percutaneous approach (Fig. 7.2).

Irrespective of the procedural modality, CA should reach lethal temperatures below -40 °C in the whole tumour mass and surrounding healthy tissue [33].

Both techniques have been widely described in the literature [35, 36].During laparoscopy (under general anaesthesia), the tumour with its surrounding fat is exposed (either trans- or retroperitoneally) and cryoprobes placed as perpendicular as possible with the tip advanced a few mm beyond the deepest margin of the tumour. The same probe

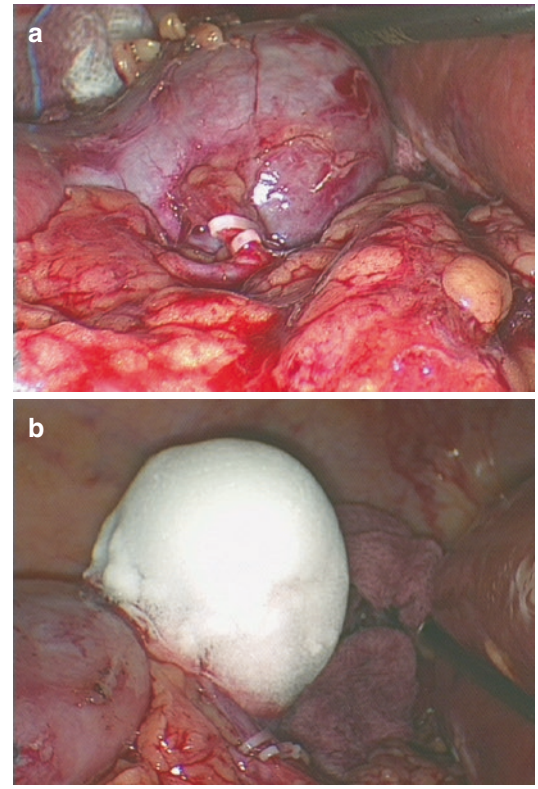

Fig. 7.2 (**a**) View of a laparoscopic-assisted cryoablation of a 3.8 cm tumour in the upper pole right kidney with an artery supply. In this case, the artery was clipped to avoid haemorrhage as no healthy kidney was supplied by this artery. (**b**) Ice ball after first freezing cycle

placement is performed under enhanced CT or MRI guidance. In both cases, thermosensors can be placed to monitor nadir temperature in the centre and periphery of the tumour. The freezing cycles have an approximate duration of 10 min, and the passive thaw is followed by some minutes of active thaw to allow for a more rapid retrieval of the needles after completing the second thaw cycle.

In order to safely perform laparoscopic CA, an intra-abdominal ultrasound probe is commonly used to assess size and position of the renal mass as well as monitor the *ice ball*, and haemostatic agents can be used in case of bleeding after probe retrieval.

During a percutaneous procedure, the *ice ball* is clearly visible by US, CT or MRI.

In both approaches, biopsy is recommended either in the preoperative setting or before

ablation intraoperatively. Procedural data shows that lethal temperatures are systematically reached in the centre of the lesion [37].

Key advantages of the percutaneous approach include that it can be performed under conscious sedation in up to 84% of the cases in some series [23]. Twenty to fifty per cent of cases require some sort displacement (hydro or gas) [22, 23, 28]. US placement of the cryoprobes can be used in order to reduce the radiation dose.

Patients treated by LCA appear to be younger, with a lower BMI and a better baseline renal function, have tumours located in the anterior valve of the kidney or in upper pole and are more likely to have multiple tumours than those treated by percutaneous approach [38]. Conversely patients treated percutaneously tend to have greater maximal tumour diameter, are frequently endophytic or in the posterior valve of the kidney and have a higher mean R.E.N.A.L. nephrometry score [38]. Shorter in hospital length of stay is the major postulated advantage of the percutaneous approach [8, 22, 23, 38].

7.4 Procedural or Technical Success and Initial Failures

Following the definitions of the working group on Image-Guided Tumour Ablation criteria [39], procedural or technical success should only be related to the procedure per se. It encompasses technical considerations as adequate placement of the probes, completion of the two freeze-thaw cycles and visual control of the ice ball extension at least 5 mm beyond the tumour limits.

When PCA is performed, a control image is usually taken at the end of the intervention by means of contrast CT. Some authors prefer to perform control imaging 24 h post procedure [28, 40]. Technically insufficient CA detected immediately after the procedure (named subtotal treatment) has been described in up to 8% of the procedures (12/147) in the series of Breen, being more frequent in the initial tertile of their experience and in multiple or upper pole tumours [36].

Regarding persistent/residual tumour rates, meta-analysis has shown that there is no statistical significant difference between laparoscopic and percutaneous procedures, rate of residual tumour per person-year 0.033 vs. 0.046, respectively, $p = 0.25$ [7].

Most of the series on LCA however proceed to the first control 3 months after the procedure. There is no doubt that the presence of enhancing regions inside or in the periphery of the tumour may translate an insufficient ablation and should be considered as a probable unsuccessful ablation (Fig. 7.3). The rate of this event is low and accounts for a maximum of 3.3% in LCA or PCA series [26, 28, 41]. However, regarding the presence of enhancement at a 3-month control, some caveats have to be considered. Size increase of the cryotherapy lesion is routinely described at 3 months, and a mild enhancement may persist on contrast CT in up to 26% of cases for as long as 12 months [42].

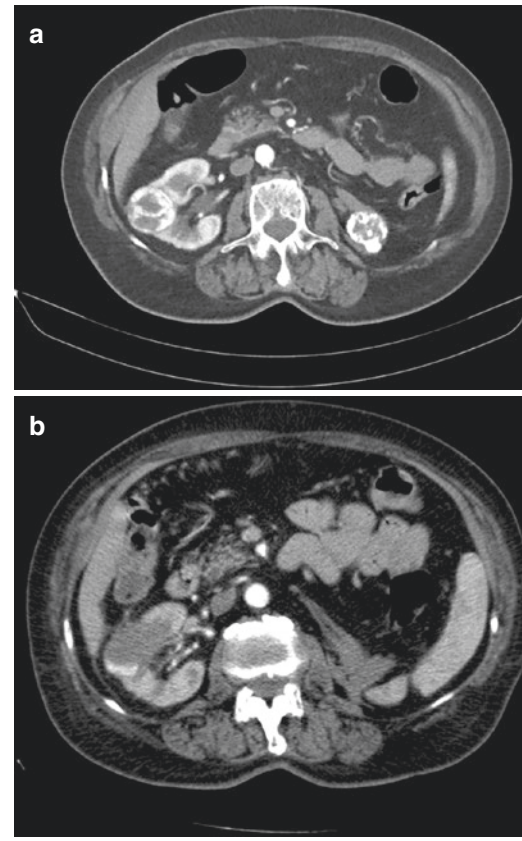

Fig. 7.3 Persistent tumour after laparoscopic cryoablation. (**a**) Initial tumour in the only functional kidney, (**b**) 3 months after LCA residual tumour posterior margin, (**c**) after second session by PCA

7.5 Perioperative Complications

Complications vary widely among series from 0 to 40% [13]. This figure can be restricted to a more realistic 8–25% when series with large sample size are analysed or in single-centre observational studies [11, 17, 35, 43, 44]. In a recent proportional meta-analysis on ablation efficacy (CA vs. RFA), a 20% of complication rate was described for CA [12]. Lower complication rate has been described for percutaneous ablation than for the laparoscopic approach by some authors [45, 46]. A critical analysis reveals that definitions and overall complication reporting have been erratic and nonstandardised and that claims of lower complication rate for PCA may not be completely sustained [38, 47]. No difference in complication rates between techniques can be definitively pronounced with the available data [7, 11]. As reported for PN [48], inconsistencies in the reporting and grading of complications may jeopardise figures for CA.

Although the majority (≈80%) of the complications in LCA seem to be Clavien Grade I–II or minor [35, 44], a meta-analysis of mostly retrospective series showed that up to half of complications may be considered major [14]. Haemorrhage and blood transfusion are reported in up to 8%, and neuralgia and flank pain attributable to probe placement may occur in up to 11% of cases either laparoscopic or percutaneous [47]. For PCA a rate between 5 and 8% of clinical significant complications, Clavien or CTCAE classification ≥3 has been described [8, 23, 28, 49].

The large series from the Mayo Clinic shows an overall complication rate of 12.2% in 311 PCAs and a major complication rate (Clavien-Dindo Grades III–IV) of 5.2% [8]. The most frequent complications were bleeding, anaemia and haematuria in 2.6%. PCA complications were of a different spectrum than the ones presented by RFA (nerve injury and urinary tract injury). The rate of complications was not significantly different from RFA [8].

Two meta-analyses show that LCA has a significantly lower likelihood of complications than PN in any modality (open, laparoscopic or robotic). Odds ratio (OR) and relative risk (RR) vary depending on the comparison arms, being at least half as common for LCA in overall, urological and non-urological categories [14, 50]. Similar meta-analytic data supports the lower complication rate of ablation when compared with minimally invasive PN [51].

7.6 Oncological Outcomes (Recurrence and Survival)

7.6.1 Short Term

The absence of recurrence or oncological efficacy is defined as persistent lack of radiological contrast enhancement and decrease in the size of the treated lesion after the first negative control [39]. Low recurrence rates in the range of 0–5% have been described by institutional series at short follow-up (median/mean lesser than 3 years) for both LCA and PCA with a median time of recurrence between 6 and 18 months [25, 28, 35, 52].

Information on short-term oncological outcomes compiled in SRs or population-based studies provide more accurate figures than those of individual series. SEER data (1998–2007) of 8818 cases of non-metastatic small RCC treated by NSS ($n = 7704$) or ablation ($n = 1114$) showed, after controlling for age, gender, tumour size and marital status, that ablation was associated to a twofold greater risk of kidney cancer death than NSS. However, predicted disease-specific survival at 5 years showed no significant differences (NSS 98.3% and ablation 96.6%) likely due to differences in OS [53].

Meta-analysis of oncological outcomes of LCA vs. PN (6785 lesions) showed a local tumour progression rate of 8.5% for LCA at mean follow-up of 29.3 months in biopsy-proven RCC. This figure represented a 5.24-fold increase in RR compared to PN. Metastatic progression in the same sub-cohort was 1.1%. While comparable to PN, mean follow-up in the PN cohort was much longer (57.3 months) [14].

More recently pooled data from the same group reported rates of local and metastatic progression following LCA of 9.4% and 4.4%, respectively. These translated into increased risks

of local (RR 9.39) and metastatic (RR 4.68) progression when compared to minimally invasive PN (laparoscopic or robotic) [50].

A meta-analysis comparing surgical versus percutaneous CA including 42 studies (1447 lesions) showed neither a statistically significant difference in the rate of residual tumour per person-year (0.033 vs. 0.046, $p = 0.25$) nor in the rate of recurrent tumour per person-year (0.008 vs. 0.009, $p = 0.44$) at a median follow-up of 15 and 13.3 months, respectively [7]. Metastatic progression was negligible in both groups at this, but the short median follow-up precluded statistical analysis [7]. Caution is recommended on drawing definitive conclusions as the rate of previous RCC is higher in CA than in PN, and a clear differentiation between local recurrence and "de novo" ipsilateral tumours has not been defined in all reports.

7.6.2 Long Term

Six series reporting on long-term outcomes on biopsy-proven RCC after ablation are included in this review [11, 38, 44, 54–56]. With a minimum and maximum median/mean follow-up of 48 and 98 months, RFS varies between 80 and 100% and CSS between 89 and 100% (Table 7.2). This long-term data supports an ipsilateral recurrence rate of ≈10% if the patient survives. Most of these local recurrences appear in the first 2 years, and late recurrences are rare. Distant metastases are rare in those patients with primary sporadic RCC (0.7–2.2% in cT1) and more frequent in those with a previous history of RCC. As expected OS is lower than CSS and varies between 76 and 95% depending on whether true data are used or 5-year estimations [11, 38, 44, 54–56].

The series of Larcher et al. provides a rigorous analysis of oncological outcomes of a solitary sporadic small renal cell carcinoma [44]. By only including cT1a masses and excluding those cases with previous history of RCC or familiar RCC syndrome, they were able to assess not only cancer-specific outcomes but also the rate of metachronous SRM-free survival in the ipsilateral or contralateral kidney (5–10-year estimates 96% and 87%, respectively) and the median time of metachronous development of SRMs (36 months). Their 5- and 10-year disease relapse-free survival (no treatment failure, no local recurrence, no metachronous SRM and no systemic progression) was 90% and 81%, respectively.

Table 7.2 Long-term oncological outcome of cryoablation in biopsy-proven RCC patients

	Approach	Patients	Follow-up	RFS %	Time to recurrence	MFS %	CSS %	OS %
Aron [54]	L	55	95 (60–133)	87 81% (5y)	24 (6–58)	89	89 92 (5 y)	84 (5y) 51 (10 y)
Barwari [11]	L	30	48 (36–63)	90	22 (6–31)	100	100	NR
Tanagho [55]	L	35	76 (SD 39.3)	80 (6 y)	27.6 (SD 11.2)	No	100 (6 y)	76.2 (6 y)
Larcher [44][a]	L	109	48 (1–156)	95 (5y) 95 (10)	18 (median)	100	100	95 (5 y) 61 (10 y)
Kim [38]	L	74	71.1(SD 35.5)	84.3 (5y)	NR	NR	98.8% (5y)	84.3 (5y)
Johnson [56]	L	67	97.9 (SD 24.8)	91[b]	39.9 (SD 39.5)	98.5	98.5 100 (5y) 98.2 (10y)	77.6 88.2 (5 y) 70.7 (10 y)

Follow-up and time to recurrence in median (SD) or mean (range) months when data is available. RFS refers to local recurrence. Time to recurrence = time to local recurrence. MFS: metastasis-free survival. (y) Kaplan-Meier survival estimation

[a]Including only SRMs and excluding previous RCC

[b]Including two cases of residual disease

Series in PCA have a shorter follow-up precluding definitive long-term conclusions. However, some Kaplan-Meier estimation is available from large series. As such 3- and 5-year local disease-free survival has been reported as 95.6% [28], and both 5-year OS and local RFS are estimated to be 86.3% according to Kim et al. [38]. Predictors of overall death were CACI ≥6 and eGFR <60 mL/min [38].

7.7 Predictive Factors for Complications and Recurrence

Recently, efforts have focused on identifying risk predictors for complications and local tumour recurrence. The incidence of perioperative complications fully justifies the analysis from a statistical point of view, and some prognostic risk factors (e.g. tumour size) have been systematically reported. However, the rates of local recurrence make it difficult to perform sound statistical analysis. Thus, the prognostic value of risk factors identified for local progression or recurrence remains uncertain.

7.7.1 For Complications

Increasing age and pre-existent morbidity have been proposed as risk factors for the development of perioperative complications [17, 35]. A large US population-based study on TA with an overall complication rate of 15% identified decreased hospital volume as a risk factor in multivariate analysis. For example, the complication rate in this study was 21% for those aged 80 or older and 24% in patients with three or more comorbidities [17].

Regarding tumour characteristics, varying cut-offs in tumour size have been identified as predictors of perioperative complications varying from 3.0 to 3.5 cm in LCA or PCA [26, 35, 47]. In PCA upper pole location predicted complications in a large series [36]. The most common complication in this series was pneumothorax known to present more frequently when the upper pole is approached by percutaneous puncture.

Besides individual tumour or patient parameters, results on defining the role of integrated tumour complexity scores as predictor of complication are controversial. The initial series of Sisul et al. assessing prognostic factors for complications after LCA or PCA included only cases with low or intermediate R.E.N.A.L. score. With an overall rate of 15% for both techniques, R.E.N.A.L. score was associated with post-procedural complications (13% in low complexity and 23.3% in intermediate). An initial model, with increasing R.E.N.A.L. score as a continuous variable, had an OR of 1.38. Nearness (N) to the collecting system was a second model predicting complications with an OR of 6.5 and 2.59 for the categories lesser than 4 mm and between 4 and 7 mm, respectively [57].

Regarding purely LCA, one multi-institutional series with an overall complication rate of 19.5% and major complication rate of 9.5% identified the R.E.N.A.L. nephrometry score as a predictive factor in multivariate analysis. Complication rates varied from 0 in cases of low-complexity tumours to 35% and 100% for moderate- and high-complexity tumours, respectively. R.E.N.A.L. nephrometry score exhibited an OR of 2.23 and predicted the risk for complications better than size alone (great area under the curve). The data was subjected to bias as only 77 from the initial 210 patients had imaging available for review, and the number of tumours in the high R.E.N.A.L. nephrometry category (9%) was very low [24].

For PCA, distribution of R.E.N.A.L. score categories matches the ones reported for LCA with a very low percentage of high-complexity tumours [25, 45]. The series of Blute et al. with a complication rate of 13% reported none and 35 and 100% of complications for low, intermediate and high R.E.N.A.L. categories. R.E.N.A.L. nephrometry as a continuous variable predicted complications with a 1.5-fold times increase per unit increase [45]. The best model predicting complications in their experience included R.E.N.A.L. score and number of probes [45]. Similar results are presented in the percutaneous ablation series of Mayo Clinic (Rochester). Among 679 procedures (of which 430 masses were treated with

PCA), major complications occurred in 5.6%. The odds of major procedural complication increased by 1.491 for each unit increase in R.E.N.A.L. score although no specific data for CA or RFA subgroups was described [25].

In addition advanced age, increased size, number of cryoprobes and central position of the tumour have been described to be associated with an increased rate of complications after PCA [8]. Nevertheless, none of the series investigating the prognostic value of anatomical complexity scores are free of limitations. Selection bias depending on imaging availability, lack of standard description of the CT scan protocols, presence of avoidable confounders in the multivariate analysis, lack of a standard definition of perioperative complications and general limitations inherent in retrospective studies mask the definitive value of R.E.N.A.L. nephrometry or PADUA score as predictors of complications in CA.

Recently a new prediction score tool has been proposed for PCA [46]. The so-called (MC)2, developed using a cohort of 398 CAs, integrates patient and tumour characteristics. Maximum tumour diameter and central tumour location were chosen as significant tumour risk factors. A history of myocardial infarction and diabetes with end organ damage were selected as patient factors. "(MC)2" score performed better than R.E.N.A.L. in predicting complications during its development and in the author's validation cohort. Pending external validation, this up-to-date score, which includes some patient risk factors for complications identified previously [35], represents the most comprehensive risk prediction score for a SRM patient population intrinsically different to that which undergoes excisional surgery [46].

7.7.2 For Oncological Outcomes

As mentioned above, any interpretation of predictive oncological risk factors is going to be hampered by a number of factors: firstly by the low rates of local recurrence or metastasis in those patients treated for sporadic RCC, secondly by the lack of homogeneity in clearly differentiating between residual and recurrent tumour and finally by the lack of series with long-term follow-up.

It is worth mentioning some of the data present in the literature. A retrospective analysis of a LCA series including a 22.8% of cases with endophytic tumours and short follow-up (median 20 months) identified endophytic growth patterns (OR 11.42) and tumour size (OR 4.09) as predictors of recurrence. However, the very low recurrence rate in this series precludes any conclusive statements [52]. A comparative study between LCA (n = 145) and PCA (n = 118) found tumour size ≥3 cm, BMI ≥ 30 and endophytic growth as predictors of local recurrence. There were no differences in recurrence rate between approaches, while CACI ≥6 and eGFR <60 mL/min were predictors of death [38]. Local failure after PCA has been significantly associated with R.E.N.A.L. nephrometry score [25] and skin to tumour distance, the latter causing a 1.5 times greater likelihood of recurrence per cm increase [45].

7.8 Renal Function Outcomes

Between 11 and 31% of patients experience some degree of loss of renal function [41, 52, 54, 58]. Overall "de novo" onset of moderate CKD at 1–2 years for patients with CKD < 3 is low.

Prospective assessments by Beemster et al. after LCA reported a mean post-ablation decline in eGFR of 7 mL/min/1.73 m^2 (median baseline GFR 82 vs. 73 mL/min/1.73 m^2) at 1 year. However, eGFR changes had minor clinical impact with only 15% of patients developing de novo "moderate" CKD ≥ 3. No patients required dialysis at a mean follow-up of 30.2 ± 16.5 months. Baseline eGFR was the only significant predictor of renal function decline after LCA. Tumour size did not have an impact on eGFR [41].

Data seems to be similar in PCA series with the percentage of patients suffering loss of renal function of any degree of 11% at 1 month, 11.5% at 3 months, 20.2% at 6 months and 26% at 1 year [22]. Conversely between 2.3 and 7% of patients may improve their basal renal function in this period showing the relative variations of the renal

function estimation [22]. A small study of patients with basal CKD ≥ 3 treated by percutaneous ablation found no significant differences between eGFR at baseline and 1 month post ablation. Renal function was maintained 1 year after ablation (41.4 vs. 44.4 mL/min/1.73 m^2), and an eGFR fall of over 25% at 1 month and 1 year, respectively, was noted in a few patients, none requiring renal replacement therapy within the study period [59].

When comparing PCA to LCA, an adequately sized study showed a similar small average eGFR decline for both techniques at the most recent evaluation. With a significantly longer follow-up for the LCA group (45.0 ± 35.4 months vs. 24.6 ± 20.0 months), similar CKD stage progression of 25% for the LCA and 28% for the PCA was observed [38].

Reports comparing functional outcomes between CA and NSS do not show statistical significant differences in post-treatment eGFR, decline in GFR or change in CKD stage between techniques [60, 61]. Similar proportional declines have been reported for CA and RAPN techniques at 1 and 6 months for some [61], while others, after controlling for tumour characteristics, found a lower mean proportional decline in the CA group (6%) than in the RAPN group (13%) [62]. New onset of CKD ≥ 3 may occur more frequently in the CA group likely to be a result of the worse preoperative renal function and older age of the ablated patients [61].

These results are comparable to institutional or multi-institutional comparative series between CA or TA in general and PN in patients with solitary kidney. The rate of patients requiring dialysis was higher for both groups (6–10%) than in the presence of a functioning contralateral kidney arms when comparing outcomes of ablation (CA and RFA) vs. open or laparoscopy PN [40, 63].

Overall the literature suggests that there is a deterioration of the renal function following CA with progression of the CKD stage in up to 25% of the cases. However, the postoperative percentage decline appears to be clinically negligible with only very few patients progressing to end-stage renal disease. The only risk factor clearly identified to influence postoperative renal function is the basal preoperative eGFR, suggesting that at least in CA, patient's factors play a more important role than tumour factors.

Conclusions

Data on CA efficacy in terms of perioperative complications, oncological and functional outcomes should be considered in the context of cohort studies and corresponding meta-analysis. The clinical profile of the CA ablation candidate differs from those of patients receiving surgery for renal mass, and some of their characteristics may affect outcomes. Complications do occur half as commonly after LCA than after minimally invasive PN. The rate of complications seems to be similar between PCA and LCA, although literature is hindered by the nonsystematic reporting of complications. Local recurrence is higher after CA than after PN although a higher percentage of cryoablated patients have antecedents of previous RCC, this factor being an important confounder. No difference in local recurrence between laparoscopy and percutaneous approach has been demonstrated. Metastatic-free survival and cancer-specific survival are comparable to PN. The role of tumour complexity scores in predicting complications or local recurrence is yet to be irrefutably demonstrated. Lastly a moderate decrease in renal function has been described after CA, with few patients evolving to severe CKD stages or necessitating dialysis.

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Open Partial Nephrectomy

8

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Abbreviations

BHD	Birt–Hogg–Dubé syndrome
HRPC	Hereditary papillary renal carcinoma
NSS	Nephron-sparing surgery
OPN	Open partial nephrectomy
OS	Overall survival
PFS	Progression-free survival
PN	Partial nephrectomy
RN	Radical nephrectomy
SRM	Small renal mass
VHL	Von Hippel–Lindau

Key Messages

- The three main goals of open partial nephrectomy (OPN) are complete removal of tumour, preservation of renal function and minimal perioperative complications.
- Standardization of the surgical technique of open partial nephrectomy along with excellent oncological outcomes and reduced morbidity has contributed to its growing application around the world.
- Preoperative and multidisciplinary care with nephrologist helps optimize renal function after partial nephrectomy.
- To minimize renal injury, small tumours can be dissected without ischaemia using manual compression by the assistant.
- OPN usually employs a flank, thoracoabdominal or subcostal incision, but a dorsal lumbotomy may also be used.

8.1 Introduction

Over the last three decades, renal cell cancer is increasingly being diagnosed at a much earlier stage than in the past [1]. This owes primarily to the widespread use of ultrasound and CT. Technological improvements in imaging

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and its easy availability have led to the increasing identification of small renal mass (SRM). It is defined as an enhancing renal tumour <4 cm in the largest dimension on imaging [2]. It has been estimated that at least 48–66% of RCC diagnoses occur as a result of cross-sectional imaging in otherwise asymptomatic patients [3]. T1a RCC has become an increasingly prevalent clinical scenario for urologic surgeons, and it has become imperative to use less invasive means of management for these masses. Nephron-sparing approaches, particularly partial nephrectomy (PN), have become increasingly popular. Although it can be performed laparoscopically and by robot-assisted PN, the greatest experience remains in open partial nephrectomy.

In the initial years, it was performed for patients with absolute indications such as bilateral RCC, RCC in a solitary kidney or RCC in the setting of pre-existing kidney disease [4]. However, lately it is being employed at tertiary-care centres for the management of localized renal tumours. Nephron-sparing surgery (NSS) is also valuable in cases of unilateral multifocal RCC and bilateral renal tumours. They are typically seen in various hereditary forms of RCC, like Von Hippel–Lindau (VHL), hereditary papillary renal carcinoma (HRPC) and Birt–Hogg–Dubé (BHD) syndromes. Bilateral and multifocal renal cancers are challenging clinical scenarios. Management strategies include concomitant bilateral PN and staged PN with either the more complex side done first or the less complex side done first. There are pros and cons of these approaches.

PN is classically done for T1a or selected patients with T1b RCC; however, several series report on the successful use of PN for tumours larger than 7 cm or with renal vein thrombus [5]. Alanee et al. reviewed contemporary series on data of 359 patients undergoing PN for T2+ RCC [6]. Median tumour size was 7.5–8.7 cm, and tumour histology was mainly clear cell. Technique was mainly open, the reported median ischaemia time was 29–45 min, and median operative time was 170–221 min. Positive margin rates were 0–31%. With a median follow-up of between 13 and 70 months, a 5-year progression-free survival (PFS) was 71–92.5%, and a 5-year overall survival (OS) was 66–94.5%. This led to a conclusion that the ability to preserve parenchyma, not tumour size, should be the main determinant of the feasibility of PN [7]. Radical nephrectomy (RN) however continued to be standard surgical approach for most renal tumours outside specialized centres. This was partly due to associated complications and concern for oncological outcomes. Most commonly encountered complications are haemorrhage, urinary fistula formation, ureteral obstruction, acute renal insufficiency and infection [8]. Van Poppel et al. compared PN (n = 2 68) and RN (n = 273) together with a limited lymph node dissection in a prospective, multicentre, phase 3 trial [9]. It was noted that PN for small, easily resectable, incidentally discovered RCC in the presence of a normal contralateral kidney can be performed safely with slightly higher complication rates than RN. Subsequent analysis of the data for oncological outcomes showed 10-year OS rates of 81.1% for RN and 75.7% for PN. With a hazard ratio (HR) of 1.50 (95% confidence interval [CI], 1.03–2.16), the test for non-inferiority is not significant (p = 0.77), and the test for superiority is significant (p = 0.03) [10]. There is considerable evidence that PN reduces the risk of chronic kidney disease (CKD) compared with RN [7]. When compared with RN, PN always provides better renal functional outcomes in similar patients [11].

Objectives of Open Partial Nephrectomy

The three main goals of OPN are:

1. Complete removal of tumour
2. Preservation of renal function
3. Minimal perioperative complications

The ideal oncological outcome for extirpative surgery is a negative surgical margin. In PN the competing key objective is to preserve renal function as much as possible. This makes PN a technically demanding procedure. Positive surgical margin in PN is defined as no cancer cells in the inked specimen [12]. Recently, Buffi and colleagues proposed a simple classification system

to identify patients with the optimal outcomes after PN procedures [13]. They combined the three main goals of PN, i.e. the negative surgical margin, <20 min warm ischaemia and minimal complications; the authors abbreviated this as an MIC. The background of the MIC system was as follows: According to this system, the goal of PN is achieved when (1) the surgical margins are negative, (2) the warm ischaemia time (WIT) is <20 min and (3) no major complications (grades 3–4 according to Clavien classification) are observed.

8.1.1 Oncological Outcomes

The standardization of the surgical technique of PN along with excellent oncological outcomes and reduced morbidity has contributed to the more frequent use of PN in many centres around the world. Oncologic results are similar to those found after RN, with better preservation of renal function [14]. Once the safety and efficacy of the procedure was established, there was the phase of expanding indications. It is classically performed in patients with multiple small RCC, bilateral RCC, RCC in patients with compromised renal function mostly in patients with T1a cancer. In select patients, even localized RCC larger than T1a can be treated with elective PN, providing good long-term outcomes [15]. For T1b RCC the data is limited, and recommendations are based on some series with carefully selected peripheral lesions. In a series of 69 carefully selected patients with >T1a peripherally located tumours, Becker noted that 55 (79.7%) had clear-cell pathology, the mean pathologic tumour size was 5.3 cm (range, 4.1–10 cm) and less than 6% experienced disease recurrence at a median follow-up of 5.8 years [15].

8.1.2 Functional Outcome

The second important goal of performing a good-quality PN is to preserve renal function. Evaluation of functional outcome however is not straightforward. The timing and method of functional assessment are less well defined in the literature. Functional impairment of the ipsilateral renal unit is multifactorial. Comorbid conditions (patient-related factors) and surgical factors (warm ischaemia time) are both important. The impact of latter is relatively straightforward and assessed by WIT. A safe WIT range is between 20 and 30 min [16]. Therefore, having a WIT <20 min can be considered a good clinical cut-off value [17]. The remnant renal parenchyma after PN is another significant predictor of postoperative renal function [18].

Yoo et al. [19] studied robot-assisted PN using warm ischaemia or OPN using cold ischaemia (CI). The authors noted that OPN was superior to robot-assisted PN in patients with a small renal mass and ischaemia time ≥25 min. However, robot-assisted procedure yielded renal functional outcomes comparable to those of open partial when ischaemia time was <25 min.

There is compelling evidence in support that even when preoperative risk factors for renal insufficiency are controlled, patients undergoing open RN are at a greater risk of chronic renal insufficiency than a similar cohort of patients undergoing PN, without compromising the oncological outcome [20]. Huang and colleagues demonstrated that the 3-year probability of absence of new-onset of glomerular filtration rates (<60 mL/min per 1.73 m^2) in a cohort of 662 patients who underwent radical/partial nephrectomy for a solitary renal tumour was 80% (95% confidence interval [CI], 73–85) after PN and 35% (95% CI, 28–43; $p < 0.0001$) after RN [8]. The authors observed that RN is an independent risk factor for new-onset kidney dysfunction.

The other surrogate markers for functional impairment are proteinuria and serum creatinine of >2 mg/dL. The Mayo Clinic experience using a matched comparison of PN and RN has shown a higher risk for proteinuria (defined as a protein-to-osmolality ratio of 0.12 or higher) and chronic renal insufficiency (defined as serum creatinine >2.0 mg/dL) after RN (risk ratio, 3.7; 95% confidence interval [CI], 1.2–11.2; $p = 0.01$) [21].

8.2 Technical Considerations

8.2.1 Indications

In order to standardize description of renal tumours, several nephrometry systems are described [22]. The two most commonly applied systems include the RENAL and PADUA nephrometry systems. They characterize anatomical features in terms of tumour radius, endophytic component, proximity to sinus fat/collecting system and location (anterior/posterior aspect and location relative to polar lines) [23]. The centrality index is the ratio of the distance between the tumour and renal centre over the tumour radius [24]. The RENAL [25] described in 2009 is perhaps the most commonly employed system and is associated with perioperative functional outcome of warm ischaemia time and estimated blood loss [26]. More recently Hsieh and colleagues [27] have described a mathematical model to determine the contact surface area of the tumour. They concluded that the contact surface area determination is a novel, reproducible, open-source and software-independent method of describing the complexity of renal tumours. It correlates with estimated blood loss and operative time and also had a better predictive value for changes in postoperative kidney compared with RENAL score.

8.2.2 Renal Ischaemia

Current evidence indicates that the use of a single cut-off for duration of ischaemia time as a dichotomous value for renal function outcomes during partial nephrectomy is flawed [28]. Current evidence has shown that patients with two kidneys undergoing nephron-sparing surgery can tolerate ischaemia times of more than 30 min without a clinically significant decline in renal function. However, every minute counts, and it is preferable to keep ischaemia time to as short as possible until clear cut-off is defined.

Small polar tumours can be resected without ischaemia; manual compression of the renal parenchyma by the assistant suffices (Fig. 8.1). Various kidney clamps have been described, but may not have any added advantage over manual compression [29]. For more complex tumours, it is preferable to have a dry field. The upper limit for warm ischaemia time is controversial; however, it should not exceed 30 min. Clamping of vessels during partial nephrectomy facilitates surgery by decreasing blood loss and improving visibility facilitating both tumour removal and renorrhaphy. Every attempt is made to limit the warm ischaemia time during partial nephrectomy. Various modifications of local parenchymal compression like manual compression, Kaufmann clamp, etc. have been described [30]. Trehan [31] in a recent meta-analysis of data from contemporary off-clamp and vessel compression series noted that off-clamp PN may be associated with improved long-term renal outcome when compared to on-clamp PN, but no difference was seen in peri- and postoperative variables, surgical complications and oncological outcomes.

Selective arterial clamping is another useful technique to reduce ischaemia and avoid reperfusion injury during partial nephrectomy [32]. This could be further improved by administering dye, commonly indocyanine green (ICG) which is injected intravenously and can be identified throughout the vascular system in less than 1 min. However, cost (requires a near-infrared camera) and debatable long-term benefit limit its use. For complex partial nephrectomy, the kidney may be cooled after clamping and the tolerable (cold) ischaemia time is significantly longer. The administration of an osmotic diuretic such as mannitol before (and after) clamping the renal vessels is often used to reduce reperfusion injury after renal ischaemia. There is, however, lack of credible data supporting the use of mannitol in the context of OPN [33]. There is controversy concerning current indications as well as optimal temperature for cold ischaemia. The two major urological association guidelines (AUA and EAU) suggest the use of hypothermia when an

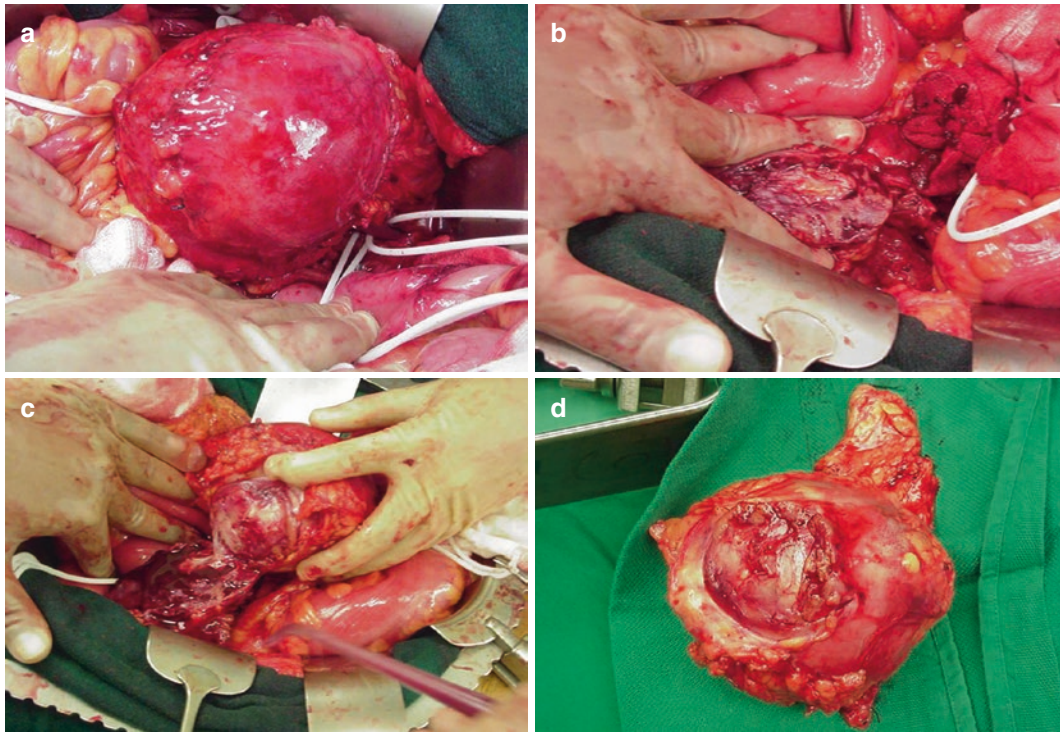

Fig. 8.1 T1b, clear-cell carcinoma of the kidney, operated via abdominal incision. (**a**) Kidney completely mobilized and vessel loos applied without clamping the vessels. (**b**) Tumour dissection along with perirenal fat and (**c**) tumour bed; haemostasis secured using manual compression only. (**d**) Specimen, see attached perirenal fat

ischaemia time (>30 min) is expected [34]. Cold ischaemia (CI) should also be kept as short as possible, ideally within 35 min. The CI technique used includes in situ cold arterial perfusion, the use of ice slush around the kidney, retrograde calyceal perfusion using cold saline or ex situ cold arterial perfusion with autotransplantation depending on preoperative findings, surgical technique (open, laparoscopic or robotic) and institutional experience [15]. In an interesting work reporting a multicentre study of 660 patients treated with warm (n = 360) or cold (n = 300) ischemic conditions in patients with a solitary kidney, authors noted that in spite of longer ischaemia during PN with cold ischaemia (median, 45 min) than with warm ischaemia (median, 22 min), the decrease in postoperative GFR (21% vs. 22%) and follow-up GFR (10% vs. 9%) was observed, confirming a protective effect of hypothermia [35].

8.2.3 Cell Saver

The kidney is a highly vascular organ, and at any given time, nearly 15% of the effective circulatory volume passes through the kidney. The blood loss during surgery for renal cell carcinoma (RCC) can be significant. Perioperative transfusion rates for partial nephrectomy may be up to 14.8% [36]. Notably, perioperative blood transfusion is an independent risk factor for decreased cancer-specific and overall survival in patients with RCC [37]. Using the Cell Saver system, which involves collection of blood lost during surgery with subsequent autotransfusion of the patient's own cells, has the potential to decrease transfusion requirement during partial nephrectomy. Lyon et al. [38] assessed if Cell Saver transfusion during open partial nephrectomy was associated with inferior outcomes with short-term follow-up, and they found that none of the

patients developed metastatic disease. It is one of the first series assessing the safety of Cell Saver during partial open nephrectomy. The data do not support the theory that intraoperative autotransfusion can lead to the rapid development of systemic metastases, and in fact we found no differences in clinical outcome between patients who did and patients who did not receive a Cell Saver transfusion. There are limitations in this retrospective work, and further work is needed to definitively determine whether the use of a Cell Saver system can mitigate the known risks associated with allogenic blood transfusion in patients with RCC.

8.2.4 Access

The standard approach for OPN employs a flank, thoracoabdominal or subcostal incision, based on the surgeon's preference and the anatomy of the mass [39]. The most commonly employed is the flank approach, particularly through the 11th rib supracostal incision. An alternative surgical approach that has been seldom explored for PN is dorsal lumbotomy. In a recent report by Tennyson et al. [40], it was noted to be associated with shorter operative times, shorter hospital stay, lower postoperative narcotic requirements and complication rates comparable. It is important to mobilize the whole kidney, so that other smaller lesions can also be identified. It is important that the prerenal fat overlying the tumour is left intact, as capsular invasion is a common finding. The renal hilum is dissected to allow application of a vascular clamp, even if no arterial clamping is envisaged. Palpation of hilar lymph nodes and para-aortic (left-sided tumours) and paracaval (right-sided cancer) should be done and any suspicious node removed and sent for frozen section.

8.2.5 Drain, Stent and Renorrhaphy

In cases of OPN, Godoy et al. suggested that drain placement might not be necessary in carefully selected patients with superficial tumours that could be removed without opening of the collecting system or after its certain closure when removing a more endophytic mass [41]. In a recent randomized trial, Kriegmair et al. [42] noted that drain placement during open partial nephrectomy can safely be omitted, even in cases with violation of the collecting system. Stents are rarely required except when there is a significant breach of the collecting system. Furthermore, dye injected through the ureter can be used to confirm complete and watertight closure of the collecting system. In case of doubt, a stent may be left in place for a few weeks. Renorrhaphy provides additional haemostasis; specific capillary bleeders should be secured and the collecting system closed. Various materials are used to bridge the renal defect; however, perirenal fat is a readily available, cheap and reliable option. The defect is closed with interrupted 3/0 Vicryl preferably on a Surgicel™ bolster to prevent sutures from cutting through the soft parenchyma. Postoperative measures are important and assessment of patients following PN. About one-fifth have acute kidney injury following PN, in a solitary kidney. However, in majority of cases, it is self-limiting and only 1% require dialysis [43].

Conclusions

Preservation of renal function without compromising the oncological outcome should be the most important goal in the decision-making process. Preoperative evaluation of several parameters, such as control of hypertension, active surveillance to detect early proteinuria and multidisciplinary care with nephrologist, helps optimize renal function after PN. Although duration of ischaemia is the surrogate marker of renal function following PN, the remaining parenchyma is an important predictor.

PN is a technically demanding procedure; however, the advantage over radical nephrectomy for T1a in terms of renal function preservation and prevention of CKD is a valid reason for using PN in most favourably located cancers. The incidence of local recurrence and even enucleation and overall and recurrence-free

survival is comparable to RN. The dissection is done in Gerota's fascia; however, peri-tumoural fat is left intact. Arterial clamping when done should limit the WIT to 20 min. In most cases of peripheral small tumours, manual and local compression suffices.

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Laparoscopic Partial Nephrectomy

9

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Abbreviations

EBL	Estimated blood loss
GFR	Glomerular filtration rate
IVC	Inferior vena cava
LPN	Laparoscopic partial nephrectomy
NSS	Nephron-sparing surgery
RALPN	Robotic-assisted laparoscopic partial nephrectomy
RCC	Renal cell carcinoma
WIT	Warm ischaemia time

Key Messages

- Imaging of the renal mass (CT or MRI) must be present at time of surgery to confirm laterality and facilitate intraoperative decision-making.
- For obese patients, all trocar ports can be shifted laterally to help facilitate visualization and mobilization of the kidney.
- Intraoperative laparoscopic ultrasonography plays a key role in identifying margin and depth of tumour and is critical in resection of larger and more endophytic lesions.
- Off-clamp approach is ideally used for smaller and peripheral lesions, while selective arterial clamping and VMD can be applied for more hilar and central tumours.
- There is no known safe threshold of warm ischaemia time as each minute sequentially contributes to risk of developing acute kidney injury and long-term decline. Renal function following LPN is dependent on quality (preoperative baseline function), quantity (number of nephrons spared), and quickness (warm ischaemia time)—Rule of three Q's.

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9.1 Introduction

Laparoscopic partial nephrectomy (LPN) has evolved substantially since Clayman et al. first described the technique in the latter part of the twentieth century [1]. Its oncologic and functional outcomes have consistently compared favourably to traditional open nephron-sparing surgery (NSS) for pT1 tumours [2–4]. Studies have shown the modality to be feasible with similar oncologic efficacy and superior renal functional outcomes compared with laparoscopic radical nephrectomy (LRN) for tumours up to pT3a [5]. Its role has been expanded to include hilar and completely endophytic tumours as well as very complex lesions [6, 7]. The main advantages of LPN include marked improvements in estimated blood loss, decreased surgical site pain, shorter postoperative convalescence, better cosmesis, and nephron preservation [8].

Over the past decade, alternative modalities to LPN have been established including laparoscopic ablative techniques and robotic-assisted LPN (RALPN). However, recent studies have demonstrated that LPN has better long-term oncologic outcomes than laparoscopic cryoablation and is more cost-efficient than RALPN [9, 10]. In experienced hands, LPN still serves as an excellent platform for NSS despite a more challenging learning curve [11]. The key principles and mainstays of LPN have remained the same regardless of modifications to the technique; these are early and secure vascular control, limited warm ischaemia time (WIT), adequate postresection haemostasis, and renorrhaphy.

9.2 Indications and Contraindications

The indications for partial nephrectomy have expanded from the so-called obligatory indications, such as lesions in solitary kidneys as well as bilateral renal tumours where nephron preservation is of the utmost importance, to elective partial nephrectomy in the presence of a contralateral normal kidney. Go et al. demonstrated the association between a reduced estimated glomerular filtration rate (GFR) and the risk of death, cardiovascular events, and hospitalization in a large, community-based population, and these findings have highlighted the clinical importance of chronic renal insufficiency [12]. Population-based studies have shifted the pendulum of renal intervention away from radical nephrectomy towards NSS in appropriately selected patients [13]. Indications also include cases of hereditary renal cell carcinoma (RCC), such as von Hippel-Lindau syndrome, hereditary papillary RCC, and Birt-Hogg-Dubé syndrome, where the risk of future development of additional renal lesions after surgery is high.

With advances in technique and growing experience, the indications of LPN have expanded beyond small (<4 cm), exophytic, and peripheral renal masses to include more technically difficult cases. Hilar and deeply infiltrating tumours in additional to tumours in solitary kidneys and larger or cystic lesions are no longer considered relative contraindications to the procedure [7, 14]. Remaining contraindications include renal vein or inferior vena cava (IVC) thrombi and significant local tumour invasion. However, in expert hands such cases can be performed [15]. Significant local tumour invasion, uncorrected coagulopathy, and inability to safely perform laparoscopy due to intra-abdominal adhesions are additional contraindications. Moderate to complete renal insufficiency is a relative contraindication to complete hilar clamping. It is important to remember that LPN is an advanced minimally invasive procedure, and considerable laparoscopic expertise and experience are both factors for successful outcomes.

9.3 Preoperative Evaluation

A complete history and physical examination must be performed as part of any preoperative evaluation. The patient should be counselled on the benefits, risks, and alternatives to kidney surgery and have a full understanding of the potential complications involved. A detailed informed consent needs to be obtained. The patient should be evaluated by the anaesthetist and medically

cleared for surgery. Laboratory studies must be performed including routine serum chemistry, full blood count, coagulation testing, and type and screen or cross-match of the patient's blood for possible intraoperative or postoperative transfusion. Anticoagulant medications (aspirin, clopidogrel, warfarin, etc.) should be discontinued at the appropriate times prior to surgery.

Imaging studies including abdominal and pelvic CT, with or without three-dimensional reconstruction, or MRI should be part of standard workup of the renal mass. If renal function is adequate, intravenous or gadolinium contrast should be administered to better define the characteristics of the renal mass as well as the vasculature. It is important to delineate tumour location, its relationship to the pelvicalyceal collecting system, and the hilar vessel architecture. The renal vein of the affected kidney and the IVC must be evaluated to be free of tumour thrombus. Additional imaging of the chest (CT or chest X-ray), bone scan, head CT, or MRI should be performed based on clinical indications in the overall workup of the patient. For centrally located tumours and for patients with haematuria, urothelial cell carcinoma must be ruled out prior to embarking on LPN. It is imperative that imaging of the renal mass is present at time of surgery to confirm laterality and facilitate intraoperative decision-making.

Mechanical bowel preparation generally is no longer needed for laparoscopic renal surgery. Studies have shown that preoperative bowel preparation does not demonstrate any perioperative benefits and can be safely omitted from routine preoperative preparations [16]. Proper hydration of the patient is necessary as euvolaemia assists in blood pressure maintenance intraoperatively given that a pneumoperitoneum usually decreases venous return. Intravenous fluid administration should be tailored to the patient's baseline cardiopulmonary and renal functional status. Euvolaemia prevents acute tubular necrosis and is essential for renoprotection in the perioperative setting.

Perioperative antibiotics, typically a first-generation cephalosporin when appropriate, should be administered within 60 min of surgical incision and discontinued within 24 h [17]. Sequential compression devices are routinely used for deep venous thrombosis prophylaxis, and subcutaneous heparin can be administered preoperatively in high thromboembolic risk patients. A Foley catheter and an oro- or nasogastric tube are placed preoperatively to maximize operating space and reduce potential for stomach and bladder injury.

Some institutions and older techniques recommend performing cystoscopy and placing an ipsilateral ureteral catheter in order to inject indigo carmine (or methylene blue) to identify collecting system entry and facilitate closure [18]. However, studies have shown that outcomes are not influenced by intraoperative identification of unrecognized collecting system entry and that postoperative urine leaks are uncommon despite recognized collecting system disruption in the majority of patients [19, 20]. Hence, it is no longer recommended to place ureteral catheters at the time of LPN.

9.4 Operating Room Preparation and Configuration

The laparoscopic approach to be used will determine the operating room configuration. Standard ergonomics dictate that the anaesthetist and anaesthetic machines are located at the head of the patient and the scrub nurse and instrument trays at the foot. Sometimes the equipment table is situated opposite the surgeon to facilitate passage of instruments, depending on surgeon preference and operating room space.

For transperitoneal LPN, the surgeon and laparoscopic camera holder (or surgical assistant) stand facing the patient's abdomen, while the viewing monitor is positioned across the patient. The viewing monitor must allow for unobstructed line of sight by the surgeon and assistant at all times during the operation. Some surgeons prefer the assistant to stand across the operative table; in these circumstances, a second viewing monitor should be placed across the assistant to the left or right of the surgeon but should not hamper his or her movement. If the retroperitoneal approach is

utilized, the set-up is largely the same except the surgeon and camera holder are at the patient's back.

9.5 Patient Positioning

The surgical approach will also dictate patient positioning. The decision to utilize the retroperitoneal approach as opposed to the transperitoneal one is based on surgeon preference and judgement based on cross-sectional imaging. A rule of thumb to determine posteriority of a kidney mass is to draw a straight line medial-to-lateral from the renal hilum to the most convex point on the lateral aspect of the kidney. Any tumour located anterior to or crossing this line theoretically may be easier to approach transperitoneally, while any tumour completely posterior to this line may be easier to approach retroperitoneally. The transperitoneal approach is used more often because it is more familiar to most urologists.

The patient is placed in the modified lateral decubitus position, which allows the bowel to fall away from the kidney and site of dissection. The transperitoneal approach is performed at or between 45 and 60° of lateral tilt, while the retroperitoneal approach is done at the full 90° tilt, which allows for easier establishment of retropneumoperitoneum. The patient should be rolled with the correct surgical side up and supported with gel rolls behind his or her back. The operating table can be flexed to maximize the space between the iliac crest and the lowermost rib; however, it is rarely necessary for the transperitoneal approach. Some surgeons may prefer to elevate the kidney rest. However, this potentially can increase risk for neuromuscular complications as well as rhabdomyolysis [21]. In any case, emphasis is placed on careful placement of foam padding at soft tissue and bony sites of pressure. This includes the head and neck, axilla, hip, knee, and ankle joints. Slight flexion at those joints can be provided to decrease the chance of inadvertent hyperextension during the surgery. A pillow is placed under both knees. An axillary roll is not required if the patient is tilted at the 45° angle and not lying directly on his or her axilla. The upper arm can be placed in a padded armrest or secured between foam cushions and placed away from the surgical site across the patient's chest with an upwards bend at the elbow. The patient is completely secured to the operating table using safety belts or silk adhesive tape, taking care to cover the skin with protective towels at tape contact points. The table should be tilted prior to start of the operation to ensure the patient is appropriately secured. The ground-return pad should be affixed to the patient's thigh.

9.6 Trocar Placement

Trocar positioning also depends on approach. A three-port placement technique is used for both transperitoneal and retroperitoneal approaches. For the transperitoneal approach, pneumoperitoneum is usually established by the closed (Veress) needle technique at the umbilicus. The primary port (10-mm) site is then placed lateral to the rectus muscle at the level of the umbilicus. A subcostal port (5/10 mm) is placed lateral to the rectus muscle and slightly inferior to the costochondral margin. The more obese the patient, the more lateral these trocar ports are placed. In thin patients, the camera port can sit at the umbilicus, and the subcostal port can sit in the midline just below the xiphoid process (Fig. 9.1a). A 12-mm working trocar is placed in the midclavicular line lateral to the camera port. We prefer to place a 12-mm Airseal System (SurgiQuest, Inc., Milford, CT, USA) trocar as the working port as the system allows us to maintain a more stable pneumoperitoneum and prevent sudden loss of insufflation pressure [22]. This valveless trocar system has been demonstrated to improve visualization by decreasing smudging of laparoscopes and evacuating smoke during cauterization, maintain pneumoperitoneum while suctioning, and allow easy extraction of specimens and needles. Insufflation gas consumption was also low, and carbon dioxide elimination was not impaired [23]. When working on the right side, an additional 5-mm trocar cephalad to the sub-xiphoid trocar can be positioned for liver retraction

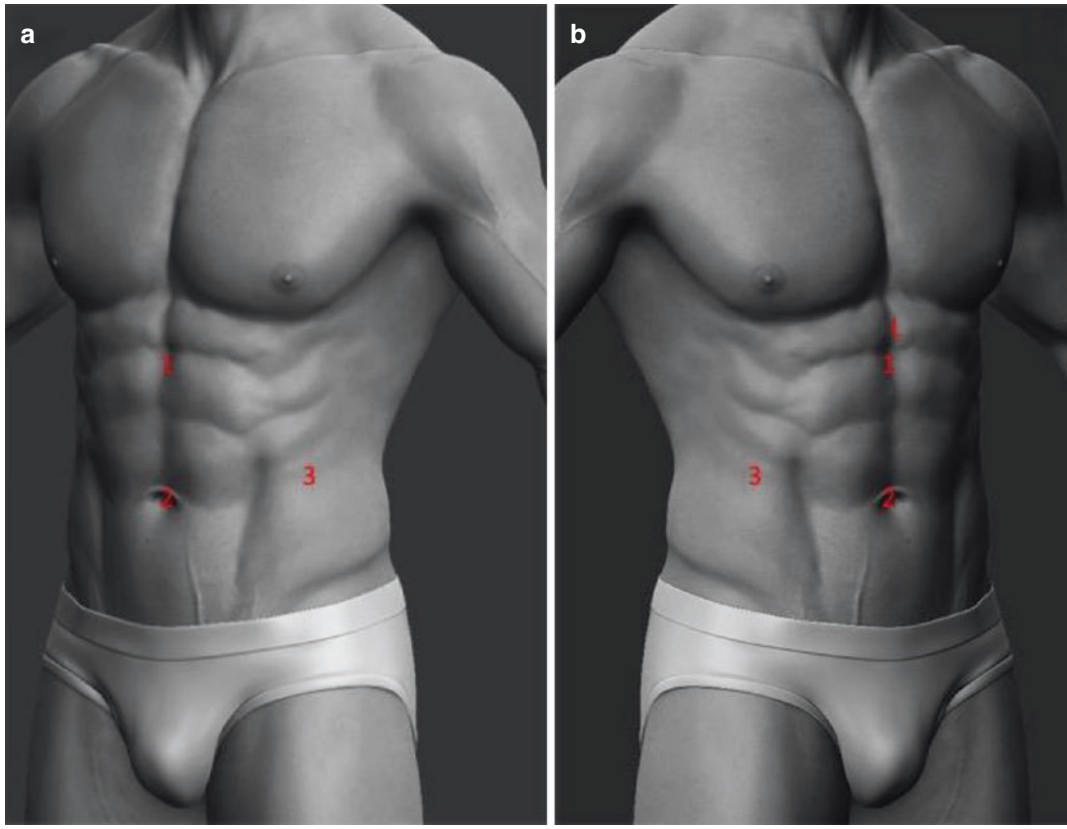

Fig. 9.1 (**a**) Trocar placement for left-sided transperitoneal LPN. *1* denotes 5-mm port, *2* denotes 10-mm camera port, and *3* denotes the 12-mm Airseal trocar site. (**b**) Trocar placement for right-sided LPN. The *L* denotes placement of the additional 5-mm trocar for liver retraction

(Fig. 9.1b). Another 10- or 12-mm trocar can be placed in the midline inferior to the umbilicus for additional access to retract the intestines medially or to place a Satinsky clamp placement if needed.

For the retroperitoneal approach, trocar insertion and placement is discussed below.

9.7 Transperitoneal Approach

After establishment of pneumoperitoneum, the colon is medially reflected along the white line of Toldt. Depending on the operative side, the retroperitoneal space is entered by adequately releasing the splenorenal or hepatorenal ligaments. On the left side, more extensive mobilization of the splenic flexure, pancreas, and spleen is required as these structures cover almost the entire anterior aspect of Gerota's fascia. On the right side, the second portion of the duodenum is carefully kocherized to expose the IVC. After the colon is mobilized and reflected, the avascular fascial plane between Gerota's fascia and the posterior mesocolon is identified and developed. Then the entire kidney is lifted upwards above this plane to identify the psoas muscle. The ureter and gonadal vein packet are found inferior to the lower pole and lateral to the ipsilateral great vessel. The gonadal vein can be ligated if interfering with the dissection, and otherwise it should be positioned medially below the site of dissection. The ureter and lower pole can be retracted upwards and laterally and traced back to the renal hilum. Dissection along the psoas muscle and lateral border of the ipsilateral great vessel leads to

the renal vein and artery. The fascia overlying the psoas muscle should remain intact during the dissection. Usually, the plane between the upper pole of the kidney and the ipsilateral adrenal gland is freed to help facilitate mobilization of the kidney and better identification of the renal hilum. Once the renal vein and artery are found, they are dissected to the extent that a window superior and inferior to each of them is created that can easily accommodate one or two laparoscopic vascular bulldog clamps.

Intraoperative ultrasound should be used to localize the lesion(s) and will help to ensure Gerota's fascia is entered away from the tumour when the kidney is defatted. Removing most of the fat from the renal surface serves to make the kidney more mobile and also allows more versatility for intraoperative ultrasound (US) viewing as well as tumour resection and suturing angles. Some fat is left on the tumours to serve as a handle during tumour resection and also to allow adequate pathological staging once the specimen is removed. Intraoperative ultrasound, using a laparoscopic transducer, helps determine the margins of the tumour and its depth. Sometimes additional lesions can be seen on US that were not previously identified on preoperative imaging. Under real-time US, the proposed line for tumour excision can be circumferentially scored on the renal capsule with the monopolar scissor around the tumour. We clamp the renal artery alone with laparoscopic bulldog clamps prior to tumour resection (Fig. 9.2a). The renal artery is clamped alone as opposed to the artery

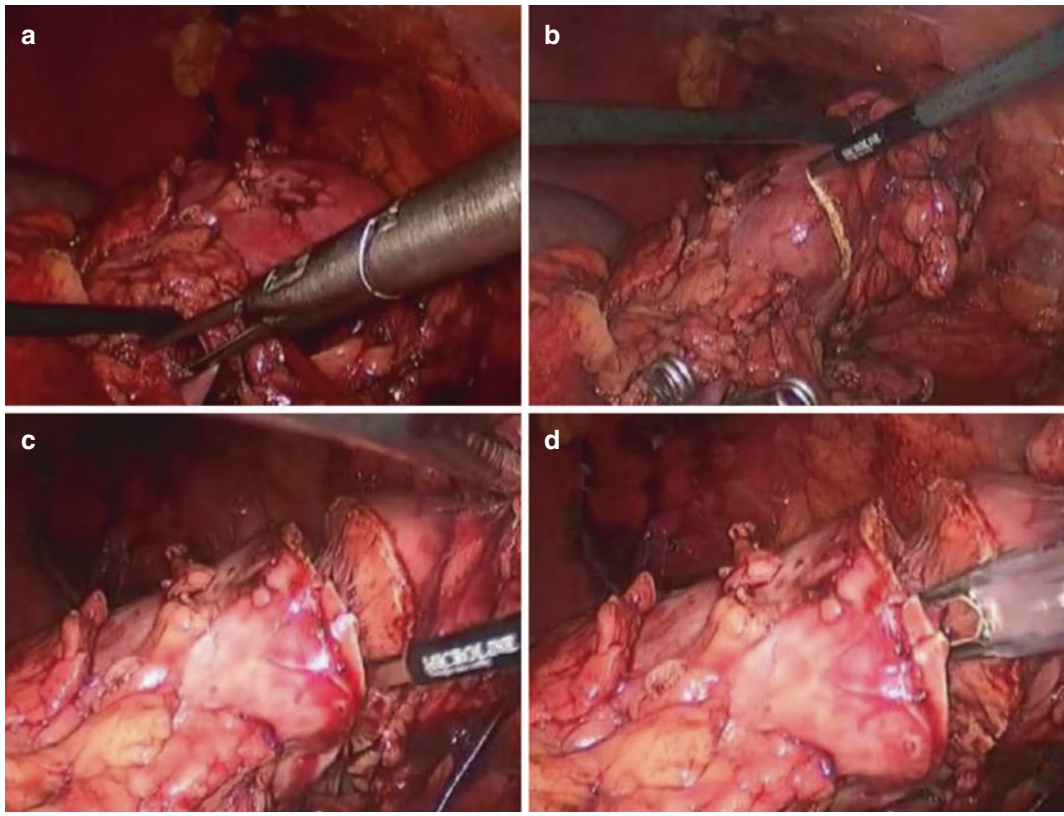

Fig. 9.2 (**a**) The renal artery is clamped with the laparoscopic bulldog clamps prior to tumour resection. Usually two are applied to ensure adequate clamping force. (**b**) The tumour can be scored with the monopolar scissor after it is identified with the laparoscopic ultrasound. (**c**) The tumour is then excised with sharp and blunt dissection with the cold scissors and suction irrigator. (**d**) Obvious arteries supplying the mass can be clipped with either metal clips or locking Hem-o-lok clips

vein clamped en bloc because it is well established that applying artery-only clamping, especially in cases with prolonged ischaemia time, lessened ischaemic renal damage during LPN [24]. A 12.5-g dose of mannitol can be given intravenously prior to hilar clamping. This has been shown in animal studies to lessen renal damage during hypoxia. However, recent studies have shown pre- and post-clamping utilization of mannitol may have no effect on functional outcomes after partial nephrectomy [25].

It is often helpful to place two bulldog clamps on the renal artery if renal artery length allows. The tumour is then excised with a combination of sharp dissection with the cold scissors, blunt dissection, and counter traction with the suction irrigator (Fig. 9.2b, c). Obvious arteries supplying the mass can be clipped with either metal clips or locking Hem-o-lok plastic clips (Teleflex, Research Triangle Park, NC, USA) as tumour excision progresses (Fig. 9.2d). Once completely excised, the mass is then placed into a 10-mm EndoCatch laparoscopic bag (Covidien, Mansfield, MA, USA) via the working port. The renal resection bed is then treated with the argon beam coagulator to aid with haemostasis (Fig. 9.3a).

Renorrhaphy can be carried out in a variety of methods. We prefer to use a 3-0 V-Loc suture (Covidien, Mansfield, MA, USA) across the base of the resection to close any collecting system or vascular injuries (Fig. 9.3b, c). A Hem-o-lok clip is applied to each end of the running suture to exert tension at the closure base. A 2-0 V-Loc

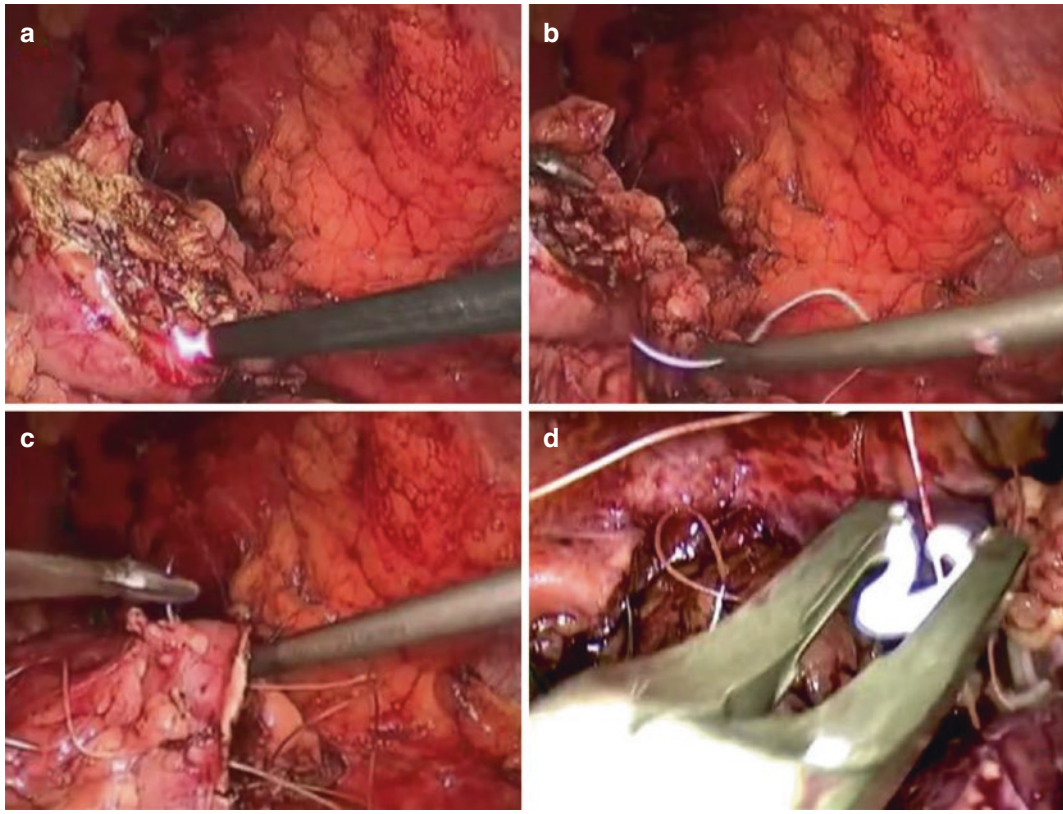

Fig. 9.3 (**a**) The resection bed can be treated with the argon beam coagulator to aid with haemostasis. (**b**) A 3–0 V-Loc suture is run across the base of the resection to close any collecting system or vascular injuries. (**c**) A 2–0 V-Loc suture follows in a continuous horizontal mattress fashion to reapproximate the renal parenchyma and complete the renorrhaphy. (**d**) A sliding Hem-o-lok clip is applied after each wall-to-wall throw to provide closing tension. The larger footprint of the Hem-o-lok clip allows for the tension to be distributed over a greater surface area

suture then follows in a continuous horizontal mattress fashion to reapproximate the renal parenchyma and complete the renorrhaphy. Alternatively, the outer renorrhaphy can be completed with a continuous running baseball stitch and a sliding Hem-o-lok clip after each wall-to-wall throw (Fig. 9.3d). Bulldog clamps can be removed after base suturing is completed to minimize warm ischaemia. Following renorrhaphy, insufflation pressure is reduced to 5 mmHg for 5–10 min to evaluate for surgical bleeding. Once haemostasis is ensured, the specimen is extracted after enlarging the camera port or working port incisions. A separate Pfannenstiel or Gibson incision may be made if the specimen is particularly large. The extraction site is determined by each surgeon's preference. A surgical drain is usually placed in the paracolic gutter adjacent to the kidney when the collecting system is entered during mass excision, although some authors contend that can be safely omitted given the low rates of urine leaks [26].

A Carter-Thomason fascial closure device (CooperSurgical, Trumbull, CT, USA) is generally used to close the 10- and 12-mm trocar sites under direct laparoscopic vision to ensure the needle passer does not injure any visceral organs and that bowel and vital structures are not entrapped within the suture. Pneumoperitoneum is released and all incision are closed at the skin level with subcuticular sutures and covered with bonding agent or adhesive strips.

9.7.1 Off-Clamp (Zero Ischaemia) Technique

Off-clamp or "zero ischaemia" approach to partial nephrectomy (PN) has been gaining popularity over the past several years and has been established to offer comparable perioperative safety, equivalent oncologic outcomes, and superior long-term renal function preservation when compared with on-clamp approach for RCC in appropriately selected patients [27]. Specifically for LPN, the technique avoids renal ischaemic injury with the benefits of minimally invasive surgery for peripheral cT1–T2 tumours [28]. Traditionally, clamping the renal hilum during LPN allows for minimal blood loss and better visualization during dissection and renorrhaphy. However, renal ischaemia and reperfusion injury are consequences of hilar occlusion. As expected, using an off-clamp technique during LPN has variably shown increased EBL when compared to hilar-controlled operations, but this does not seem to translate into increased risk of transfusion or loss of visualization leading to compromise in oncologic outcomes [29]. Intraoperatively, an emphasis is placed on completely mobilizing the kidney and defatting the tumour to allow an unhindered view during resection and suturing. Adequate suctioning must be readily available, and an argon beam applicator can be used to coagulate the deep resection bed. Some authors have even advocated using thulium laser as a method for resection during zero ischaemia or superselectively embolizing tumour vessels prior to LPN to improve haemostasis [30, 31].

9.7.2 Selective Arterial Clamping

Gill et al. first described the technique of anatomic vascular microdissection of renal artery branches to allow selective clamping of vessels to extend the application of zero-ischaemia PN [32].This allowed more complex tumours such as hilar, central, intrarenal, and polar lesions to be resected without global surgical renal ischaemia. After exposure of the renal hilum, the main renal artery and vein are circumferentially mobilized and encircled with vessel loops. After assessing the patient's preoperative CT-reconstructed three-dimensional hilar architecture, microdissection is performed in a medial-to-lateral direction to identify the specific arterial branch(es) supplying the tumour. Additional vessel loops are used to isolate and retract higher-order arterial branches during vascular microdissection. A small nephrotomy may be necessary as dissection approaches the tumour—the incision is made on the hilar edge of the kidney overlying the anterior surface of the arterial branch. Microsurgical bulldog clamps are used to clamp the targeted arterial branches, and evaluation of the renal parenchyma

surrounding the tumour is performed to confirm normal colour and turgor. If there is concern the clamped branch has reduced perfusion to normal kidney, the bulldog is removed immediately. Arterial mapping with this superselective ligation approach is done until only branches to the tumour(s) is clamped, and the rest of the kidney is free from ischaemia. The use of a laparoscopic Doppler can also help with identification of target arterial branches; cessation of intratumoural and peritumoural arterial flow confirms that the correct arterial branch has been controlled. Resection of the tumour(s) then takes place in the standard fashion as described above.

9.8 Retroperitoneal Approach

A retroperitoneal approach to laparoscopic partial nephrectomy is most beneficial for posteriorly located masses and in instances where considerable intraperitoneal adhesions are anticipated. Because of the limited working space and fewer familiar landmarks, the retroperitoneal approach can prove challenging particularly in obese patients with considerable retroperitoneal adiposity and in patients with perirenal scar tissue from prior renal surgery or infections.

Following induction of anaesthesia, an orogastric tube and urethral Foley catheter are placed as in the transperitoneal approach. The patient is then placed in the full flank (lateral decubitus) position with the ipsilateral tumour side up as described above.

Port placement is described as above. A 15-mm incision is made at the tip of the 12th rib half way between iliac crest and the rib in the midaxillary line (Petit's triangle). This is carried down through the subcutaneous tissue, abdominal sidewall musculature, and lumbodorsal fascia until the retroperitoneal space is entered. A 10-mm camera trocar is placed through this entry port. The surgeon's finger can then be used to begin to bluntly develop the retroperitoneal space. The fat overlying the psoas should be cleared by sweeping it anteriorly and cephalad towards the kidney. Care should be taken to avoid entering Gerota's fascia when performing this manoeuvre. Next, a balloon dilator can be inserted into this space and inflated to 500–800 mL. During this step the ureter and ipsilateral gonadal vessels can often be seen above the psoas muscle in patients with limited retroperitoneal fat tissue. Certain balloon dilators will accommodate the laparoscopic telescope allowing inflation to be done under direct vision. The camera trocar is then placed through this entry tract and the retroperitoneum insufflated to 15-mm Hg pressure with carbon dioxide gas.

Alternatively, the laparoscope can be placed through a 10-mm or 12-mm visual obturator trocar fitted with a retractable blade allowing retroperitoneal entry under direct vision. When traversing the muscle layers of the abdominal sidewall, ensure that the blade of the visual obturator is parallel to the muscle fibres. This facilitates trocar tunnelling and minimizes muscle bleeding.

An additional 10-/12-mm working trocar (or 12-mm AirSeal trocar) is placed posteriorly, under the 12th rib, just lateral to the spinous musculature and positioned approximately 2 cm cephalad to the camera port. It is often necessary to reflect the peritoneum medially to create space to place a 5-mm port in the anterior axillary line off the tip of the 11th rib. An additional 5-mm trocar can be placed off the tip of the tenth rib. It is especially important to directly visualize medial port placement to ensure the peritoneum is not violated and thus reduce the risk of inadvertent bowel injury.

During the retroperitoneal approach, the psoas muscle and tendon act as the most reliable landmarks and should be oriented horizontally and inferiorly. The peritoneal reflection should be visible anteriorly and Gerota's fascia located in the cephalad direction. The ureter is often located just medial and anterior to the psoas muscle tendon. Similar to the transperitoneal approach, identification of the ureter is crucial to avoid unrecognized injury and can be traced superiorly to the renal hilum. The kidney and ureter should be retracted cephalad and upwards to place the renal hilum on stretch and ease its dissection. When approaching the hilum, the

renal artery is usually encountered first from the retroperitoneal approach. The renal artery pulsation is frequently visible through the perihilar fat and helps guide dissection in this area. The artery and vein are then isolated enough to ensure safe placement of hilar clamps (e.g. laparoscopic bulldogs). The surgeon must bear in mind that just medial to the ureter lies the aorta when performing a left partial nephrectomy and the inferior vena cava when performing a right-sided partial nephrectomy.

Similar to the transperitoneal approach, intraoperative ultrasound should be utilized to localize the renal mass. Gerota's fascia should be entered away from the mass, and perirenal fat should be cleared down to the renal capsule circumferentially around the planned excision site. Perirenal fat directly over the mass should be left intact if at all possible and sent with the specimen for pathological analysis. Ultrasound is again used to confirm tumour location and assess tumour depth and configuration. Then renal capsular incision is then scored with cautery. Next, the renal hilum is controlled with laparoscopic bulldog clamps. Resection of the mass and subsequent renorrhaphy takes place in similar method as described for intraperitoneal LPN.

9.9 Postoperative Management

A complete blood count, urea and electrolytes, and creatinine are usually obtained in the recovery room, but not necessary for every LPN case. These labs are repeated 12 h postoperatively. It is important to keep in mind that postoperative haemorrhage remains a critical complication of the operation. Vital signs and quantity as well as quality of drainage outputs should be carefully monitored overnight as haemorrhage may manifest as low urine output, gross haematuria, copious bloody output from surgical drain, and haemodynamic instability.

Most institutions recommend 12–24 h of bed rest with patients ambulating by the morning of postoperative day 1 [33]. Some authors will recommend even earlier ambulation in order to prevent deep vein thrombosis. Both prophylactic doses of subcutaneous heparin as well as compression stockings should be applied immediately postoperatively. In patients at particularly high risk for DVT, preoperative prophylactic dosing of subcutaneous heparin or enoxaparin should be considered. We recommend restraint in terms of exercise and extraneous physical activities for at least a month to facilitate adequate healing of the resection bed.

In general, any oro- or nasogastric tube is removed prior to extubation, and the patient is given a clear liquid diet in the recovery room once fully awakened from anaesthesia. The diet is continued or advanced the next morning depending on clinical indications. The Foley catheter is kept overnight to measure outputs and removed the next morning. Drain output volumes are meticulously monitored after Foley removal because any significant increase may represent vesicoureteral reflux into a persistent or unrecognized collecting system injury. The creatinine concentration of the drain fluid is analysed and compared to the serum creatinine level to assess for urine leak and to help determine the timing of drain removal. The Foley catheter may be reinserted if output from surgical drain is suggestive of urine leak and if volumes are significant.

Most patients are discharged home postoperative day 1 or 2 without any external tubes. Patients are provided with a bowel regimen and narcotic pain medication to take as needed. For pT1 tumours, LPN patients are followed with abdominal imaging (CT or MRI) within 3–12 months postoperatively, in addition to chest X-ray and laboratory studies, as per AUA surveillance guidelines [34].

9.10 Surgical Complications

Intraoperative complications usually are associated with inadequate vascular control such as clamp failure, inability to identify and control multiple renal arteries, or poor haemostatic control during base-layer suturing and renorrhaphy. In larger studies, intraoperative haemorrhage can range as high as 3.5% and require conversion to

open in 1% [33]. Additional less common injuries can occur to the ureter, bowel, spleen, liver and gallbladder, pancreas, and great vessels.

Postoperative complications are typically related to bleeding or urine leak. Delayed spontaneous haemorrhage can occur up to 30 days postoperatively and has a reported frequency as high as 9.5%. The incidence of urine leak is approximately 4.5% [33]. Conservative management, selective angioembolization, or completion nephrectomy are the treatment options depending on clinical severity. Collecting system injuries rarely require reoperation with most resolving spontaneously and less than 10% needing urinary diversion (by either ureteral stent or percutaneous nephrostomy) [33].

9.11 Oncologic Outcomes

The trifecta of negative cancer margins, preserved renal function, and minimal perioperative complications—goals that are essential for open partial nephrectomy—has been well translated to LPN across the urologic literature [35–37]. Positive surgical margins for most LPN series remain less than 1% with cancer-specific survival (CSS) of over 95% and 90% at 10 years for cT1a and cT1b RCC, respectively [2]. The role and indications of LPN have been expanded to much more complex tumours—hilar, completely endophytic, and T1b and larger—and technical modifications have improved WIT and overall renal function preservation. LPN remains a valid alternative to OPN and a viable modality despite rapid technological advancements in robotics and ablative therapies.

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Robot-Assisted Partial Nephrectomy

10

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Abbreviations

EBL	Estimated blood loss
eGFR	Estimated glomerular filtration rate
LPN	Laparoscopic partial nephrectomy
PN	Partial nephrectomy
RAPN	Robot-assisted partial nephrectomy
WIT	Warm ischaemic time

Key Messages

- RAPN in the hands of expert surgeons is associated with excellent outcomes in terms of perioperative complications and functional results.
- RAPN could also be indicated in complex tumours, including hilar lesions, bilateral tumours, tumours in solitary kidney, or tumours in kidneys previously treated with partial nephrectomy.
- Special complex indications must be reserved to very experienced surgeons.
- The natural history of the small renal masses typically treated with RAPN as well as the short-term follow-up available in the published studies due to the relatively recent development of the procedure prevent definitive conclusions on the oncological outcomes.

10.1 Introduction

Historically, radical nephrectomy has been considered the gold standard for localised renal carcinoma. Partial nephrectomy was initially limited to absolute indications such as patients with bilateral RCC or a solitary kidney and relative indications such as impaired renal function in the contralateral kidney. With growing experience in the surgical technique, the procedure has been

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subsequently adopted in elective indications, i.e. patients with a single tumour in one of the kidney with contralateral healthy kidney, with the purpose to preserve healthy renal parenchyma and maintain good renal function. Currently, according to all the urological guidelines, elective partial nephrectomy is indicated in tumours smaller than 4 cm, whenever it is technically feasible, in the presence of a healthy contralateral kidney [1].

Initially, partial nephrectomy (PN) was predominantly performed with an open approach. More recently, minimally invasive approaches (i.e. pure laparoscopy or robot-assisted laparoscopy) have gained widespread popularity and have been increasingly applied to PN. However, pure laparoscopic partial nephrectomy (LPN) is a challenging procedure with a long learning curve. The procedure requires delicate extirpative and reconstructive oncological surgery, with negative surgical margins, in one of the most vascularized human organs and in the shortest time possible in order to reduce warm ischemia time [2]. The dissemination of the da Vinci surgical system has allowed increased adoption of robot-assisted partial nephrectomy (RAPN) in the treatment of small renal tumours. This chapter highlights the main data concerning the different surgical steps of RAPN and the main results available in the literature.

10.2 Surgical Technique

10.2.1 Conventional Multiport vs. Single-Site Robot-Assisted Partial Nephrectomy

Single-site surgery has been developed in the last few years in order to provide less port-related complications, quicker recovery time, less pain and better cosmesis, due to the minimization of skin incisions to gain access to the abdominal or pelvic cavities [3]. Although the technique has been applied to RAPN only in selected cases and by experienced surgeons with promising results [4], a recent comparative study evaluating multiport vs. single-port RAPN demonstrated significantly better outcomes for standard multiport RAPN in terms of operative time, warm ischemia time (WIT) and postoperative estimated glomerular filtration rate as well as in achieving the trifecta outcomes (defined as WIT less than 25 min, negative surgical margins and no intraoperative or postoperative complications) [5]. Hence at the present time and with the currently available da Vinci platform, there is only a limited role for single site in RAPN.

10.2.2 Transperitoneal vs. Retroperitoneal Approach

RAPN is more commonly performed through a transperitoneal approach. However, the retroperitoneal approach has been described in several surgical series [6]. The main advantages of retroperitoneal approach include avoiding bowel mobilisation, more direct access to kidney and renal hilum as well as potentially easier dissection of posterior tumours, with the potential to decrease operating time. Conversely, the main disadvantages are characterised by the small working space and the presence of restrictive landmarks. Although comparative studies with transperitoneal and retroperitoneal RAPN are sparse, a recent systematic review and meta-analysis on LPN demonstrated shorter operating time (weight mean difference 48.85 min; $p < 0.001$) and shorter length of hospital stay (weight mean difference 1.01 days; $p = 0.001$) in favour of the retroperitoneal approach [7]. The validity of those figures for RAPN remains unclear, and the selection between the two approaches is mainly based of surgeon preference and tumour location.

10.2.3 Hilar Control

The classic approach to RAPN includes clamping of the main renal artery in order to reduce blood loss and allow tumour resection in a bloodless field. The vascular clamp is typically removed at the end of the cortical renorrhaphy. More recently, Gill et al. reported an early unclamping technique, whereby artery clamps

are removed after closure of the inner medullary defect, allowing significantly reduced WIT [8].

Due to the increased relevance of WIT as modifiable factor to reduce kidney injury and loss of renal function, alternative approaches have been reported. Off-clamp RAPN has been described in selected cases with of non-complex tumours and large exophytic growth (e.g. low RENAL nephrometry or PADUA scores), demonstrating good perioperative results and preservation of the renal function [9]. More recently, a super-selective clamping of tertiary or higher-order arterial branches has been described by Gill et al. in order to provide ischemia of the tumour without compromising blood flow in the remaining parenchyma in complex tumours not suitable for off-clamp techniques [10, 11]. Specifically, a detailed preoperative 3D reconstruction of triphasic CT images of the kidneys with 0.5-mm thickness slice acquisition is performed to evaluate tumour and vascular anatomy accurately. Intraoperative vascular microdissection of secondary, tertiary and quaternary branches is performed in order to identify specific vascular branches directly supplying the tumour, which are clip-ligated and divided. Conversely, tertiary or quaternary branches supplying the peri-tumoural parenchyma are selectively and transiently controlled with a neurosurgical micro-bulldog clamp during tumour excision. Intraoperative colour Doppler ultrasound is performed before tumour resection to confirm the absence of blood flow within the tumour as well as a reduction in peritumoural blood flow [8, 9]. Alternatively near-infrared fluorescence imaging can also be adopted to demonstrate the efficacy of the super-selective clamping before tumour resection [12].

In the most recent publication by the same group comparing such sophisticated technique with the standard artery clamping, the authors demonstrated that super-selective clamping was associated with longer median operative time ($p < 0.001$) and higher transfusion rates (24% vs. 6%, $p < 0.01$) but comparative perioperative complications (15% vs. 13%) and hospital stay. However, patients receiving super-selective clamping experienced significantly less reduction in estimated glomerular filtration rate at discharge (0% vs. 11%, $p = 0.01$) and at last follow-up (11% vs. 17%, $p = 0.03$) as well as greater parenchymal preservation on postoperative CT volumetrics [13]. Although extremely appealing, vascular microdissection and super-selective clamping are extremely complex surgical techniques, whose reproducibility outside of the centre which initially promoted has not been extensively tested.

As an alternative technique to performing minimally invasive partial nephrectomy without artery clamping in complex tumours, preoperative super-selective transarterial embolization or intraoperative controlled hypotension have been reported [14, 15], but the use of either techniques remains limited. Finally, cold ischemia has been also adopted during RAPN either by transarterial cold perfusion of the kidney, by retrograde ureteral cooling or, more recently, by the use of ice slush to cover the kidney during ischemia time [16].

10.2.4 Tumour Identification and Excision

Although not mandatory in the presence of predominantly exophytic tumours, margin identification and marking by intraoperative ultrasound are of particular use in case of neoplasms with large endophytic components and/or proximity to the hilum (Fig. 10.1). Robotic ultrasound probes

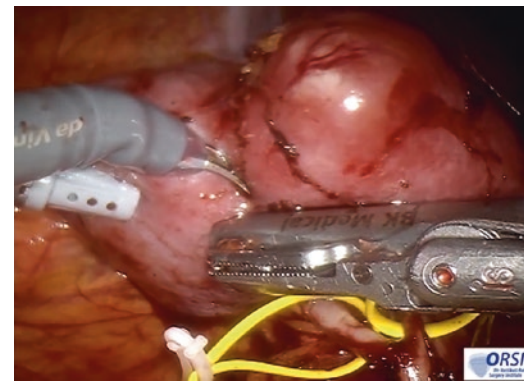

Fig. 10.1 Demarcation of the tumour (cT1b, >50% exophytic, PADUA score 8 lesion) by intraoperative ultrasound

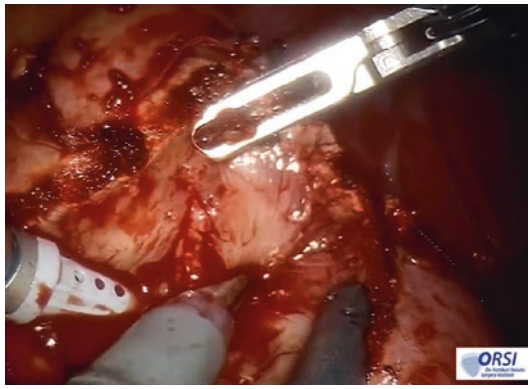

Fig. 10.2 Sharp dissection preserving a rim of healthy parenchyma on the tumour margin free of any cautery. Note the robotic suction device adopted in the dual console system in order to improve suction and countertraction during resection of the tumour (same case as Fig. 10.1)

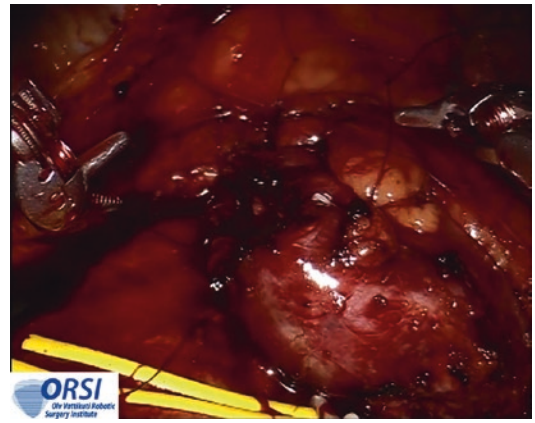

Fig. 10.3 Resection bed after inner renorrhaphy and early unclamping. A running Monocryl 3-0 suture preloaded with a Hem-o-lok clip is brought outside through the parenchyma and secured with a Hem-o-lok clip at the end of the renorrhaphy

are available, allowing direct control of the probe by the console surgeon [17].

Tumour excision should be ideally performed sharply with a rim of normal renal parenchyma, mainly using cold scissors, in order to better visualise the healthy surrounding parenchyma and minimise the risk of positive surgical margins (Fig. 10.2). In order to allow off-clamping dissection, a variety of lasers have been tested in tumour excision, including thulium, CO_2, Green Light and diode lasers [18–20]. Although promising, laser excision is not currently regarded as a standard technique, likely due to the lack of the ideal laser.

10.2.5 Renorrhaphy

Renorrhaphy is typically performed according to the sliding clip technique, originally described by Benway et al. [21]. Specifically, the inner medullary defect is closed with a running Monocryl 3-0 suture preloaded with a Hem-o-lok clip, taking all retracted calices and vessels in the running suture. On closing the Monocryl is brought out through the parenchyma and secured with a Hem-o-lok clip. The sliding clip technique allows the right tension and can be brought onto the suture (Fig. 10.3).

Various fibrinogen coagulation enhancers and tissue sealants (e.g. Floseal) can be used on the defect, together with bolsters. However, their usefulness is questionable (Fig. 10.4). Monopolar or bipolar cautery can be applied on the cortex of the resection bed. The borders of the defect are closed with polyfilament 1-0 sutures. According to the surgeon's preferences, either interrupted sutures or, more commonly and quicker, a running suture secured with a Hem-o-lok clip at each bite can be used and proper tension applied to the tissue. Subsequent tension readjustments can be made [21, 22] (Fig. 10.5). Notably, some surgeons have advocated avoiding cortical renorrhaphy in order to reduce the risk of renal function loss. However, clinical data on the benefits and risks of this technique are still awaited.

10.3 Results

LPN remains a challenging procedure. In a single surgeon series of 800 cases performed by one of the pioneers of LPN who also has the largest experience in the field, Gill et al. demonstrated mean WIT of about 32 min over the first 500 cases performed, with WIT shorter than 20 min in only 15% of cases [8]. Moreover, complication rates were as high as 24% in the first 275 cases

Fig. 10.4 Application of a haemostatic agent (PerClot®) at the end of the cortical renorrhaphy (same case as Fig. 10.1)

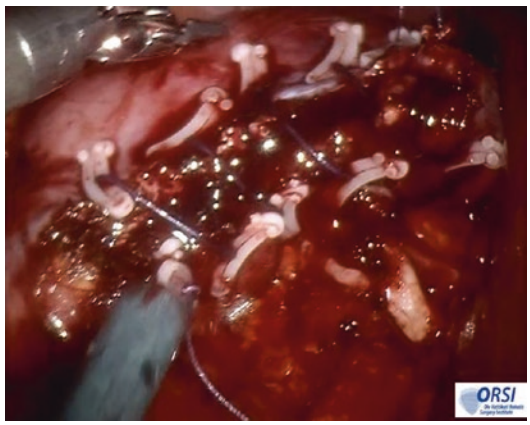

Fig. 10.5 Appearance of the kidney at the end of the cortical renorrhaphy (same case as Fig. 10.1)

and only decreased to 15% in the subsequent 289 cases [8]. Taken together, these data suggest that, even with an overwhelming surgical volume which is impossible to achieve for most laparoscopic surgeons, the procedure is associated with a high risk of complications and a long WIT. Consequently, it is not surprising that population-based studies suggest that the adoption of LPN is not widespread, being used in only 9% of all the partial nephrectomy cases performed in the USA from 2008 to 2010, as reported in the Nationwide Inpatient Sample dataset [23].

Due to the da Vinci surgical system, RAPN may offer significant advantages over conventional LPN. Two recently reported systematic reviews and meta-analyses compared the outcome of LPN and RAPN. Froghi et al. [24] reported a meta-analysis of six non-randomised comparative studies [25–30] evaluating RAPN and LPN in the treatment of T1a small renal mass. Two hundred fifty-six patients were included in analysis which demonstrated that all the perioperative outcomes, including WIT and complication rates, were similar between LPN and RAPN [24]. Subsequently, Aboumarzouk et al. [31] reported a study with similar methodology, evaluating seven non-randomised observational studies [26, 29, 30, 32–35] and included more than 300 RAPN and 400 LPN cases. RAPN was found to be associated with significantly lower WIT (mean difference 2.7 min; 95% confidence interval 1.1–4.3 min; $p = 0.0008$). Conversely, operative times, estimated blood loss, conversion rates, complication rates and postoperative length of hospital stay were similar in the two groups [31]. Notably, despite similar inclusion criteria and designs, the two systematic reviews identified different studies, with only three papers [26, 29, 30] being included in both analyses. This clearly suggests that the systematic searches at the bases of both reviews were not sufficiently sensitive. Nevertheless, virtually all included studies were of poor methodology, due to lack of randomisation and small sample sizes which prevented definitive conclusions to be made (Table 10.1). For example, most of the studies included in the meta-analyses included patients treated by surgeons in the initial phase of their RAPN learning curves, as demonstrated by the limited volume of RAPN cases included in analyses. It is well known and accepted that, even for surgeons with previous robotic experience, RAPN outcomes over the course of at least the first 50 cases [22]. Consequently, clinically speaking, the only concept which can be derived from both reviews is that, even during the learning curve, RAPN already resulted in equal perioperative outcomes to LPN performed by more experienced laparoscopic surgeons [36].

Mature series of RAPN have provided more insights on the huge potentiality of this surgical approach. In a multicentre series of almost 350 cases of RAPN performed in four European and US high-volume referral centres, Ficarra et al.

Table 10.1 Comparative studies reporting outcomes of RAPN and LPN

Authors	Study design	Cases	Tumour size (cm)	Mean operative time (minutes)	Median/ Mean blood loss (mL)	Mean warm ischemia time (minutes)	Overall complication rate (%)	In-hospital stay (days)	Positive surgical margins (%)
Aron et al. 2008 [25]	Retrospective	RAPN 12 LPN 12	2.4 2.9	242 256	329 300	23 22	—	4.7 4.4	0 0
Jeon et al. 2009 [34]	Retrospective	RAPN 31 LPN 26	3.4 2.4	170 139	198 208	20.9 17.2	—	5.2 5.3	3 0
Kural et al. 2009 [26]	Retrospective	RAPN 11 LPN 20	3.2 3.1	185 226	286 387	27 36	—	3.9 4.2	0 5
Haber et al. 2010 [33]	Retrospective	RAPN 75 LPN 186	2.7 2.5	200 197	323 222	18 20	16 13	4.2 4.1	0 0
Hillyer et al. 2011 [27]	Prospective	RAPN 9 LPN 17	2.8 2.7	—	225 175	19 37	22 23	4 4.5	0 0
Lavery et al. 2011 [28]	Retrospective	RAPN 20 LPN 18	2.5 2.3	189 180	93 140	23 25	15 11	2.6 2.9	0 0
Pierorazio 2011 [35]	Retrospective	RAPN 48 LPN 102	2.2 2.5	152 193	122 245	14 18	10 17	2 2	4 1
Seo et al. 2011 [30]	Retrospective	RAPN 13 LPN 14	2.7 2	153 117	284 264	35 36	15 0	6.2 5.3	0 0
Williams et al. 2011 [29]	Prospective	RAPN 27 LPN 59	2.5 3	233 221	180 146	18 28	18 20	2.5 2.7	4 12
Ellison et al. 2012 [32]	Prospective	RAPN 145 LPN 204	2.9 2.7	215 162	368 400	25 19	33 20	2.7 2.2	7 7

Modified from [24, 31]

demonstrated that WIT <20 min was achievable in 64% of the cases (with median WIT of only 18 min) and overall complication rates as low as 12% (and only 3% of high-grade complications) [37]. In another multicentre series, comprising 450 cases from 4 institutions, Spana et al. demonstrated an overall prevalence of complications of 15.8%, with most of the complications being of Clavien grades 1 or 2 and only 3.8% major complications [38].

Dulabon et al. analyses a large multicentre series from four high-volume, US referral centres evaluating the outcome of RAPN in hilar tumours [39]. In this cohort of complex tumours, with a mean diameter of 3.6 cm, RAPN as performed by experienced surgeons was associated with mean WIT of 26 min, no risk of conversion to open or laparoscopic partial nephrectomy, no loss of renal unit, low risk of complications (2.4% of Clavien grade 2 complications) and very low risk of positive surgical margins (2%) [39].

Moreover, in two other large multicentre series, Ficarra et al. [40] and Petros et al. [41] demonstrated that RAPN was feasible in cT1b tumours, with acceptable mean WIT (22 and 24 minutes in the two studies, respectively) and low risk of intraoperative (4% and 0%, respectively) and postoperative high-grade complications (about 8%) [40, 41]. Notably conflicting results have been reported in other series [42–44] (Table 10.2).

Finally, the accuracy of RAPN makes the procedure feasible with good perioperative and functional results even in patients with baseline chronic kidney disease. In another multi-institutional collaboration, Kumar et al.

Table 10.2 RAPN surgical series for cT1b renal mass

Authors	Cases	Tumour size (cm)	Mean operative time (minutes)	Median/Mean blood loss (mL)	Mean warm ischemia time (minutes)	Overall complication rate (%)	Positive surgical margins (%)	Estimated glomerular filtration rate decrease
Ficarra et al. 2012 [41]	49	5	177	120	22	26	5	7
Petros et al. 2012 [42]	83	5	194	200	24	8	0	9
Patel et al. 2010 [43]	15	5	275	100	25	27	0	12
Gupta et al. 2013 [44]	17	5	390	500	36	6	0	5

Modified from [44]

demonstrated that RAPN in patients with baseline chronic kidney disease was associated with a higher risk of complications as compared to a matched population of patients with normal renal function undergoing the same procedure [45]. However, patients with pre-existing chronic kidney disease experienced a more limited decline of glomerular filtration rate [45].

Few studies evaluated the efficacy of RAPN in very challenging cases, such as hilar tumours, totally endophytic lesions, large tumours (≥4 cm), tumours in solitary kidney, multiple unilateral or bilateral tumours and local recurrences after previous PN.

With regard to hilar tumours, Dulabon et al. compared 41 patients with hilar renal masses with 405 patients without hilar masses. They demonstrated that RAPN is a safe, effective and feasible option in such a complex category of tumours. Specifically, only WIT was significantly longer in hilar tumours than in the non-hilar group (26.3 min vs. 19.6 min; $p < 0.0001$), whereas no others differences in other perioperative or postoperative outcomes and pathologic surgical margin rate were found [39]. In 2013, Eyraud et al. compared 294 non-hilar tumours and 70 hilar ones treated with RAPN by an expert surgeon. In this series, hilar location for patients undergoing RAPN in a high-volume institution seems not to be associated with an increased risk of transfusions, major complications or decline of early postoperative renal function. Specifically, the authors reported longer operative time, longer WIT and increased estimated blood loss (EBL) in hilar tumours. Conversely, no differences were noted in terms of complications and positive margins as well as in postoperative eGFR at last follow-up. WIT was the only perioperative outcome influenced by hilar location in multivariable analysis [46]. Recently, in a single centre study evaluating 44 cases with a PADUA score ≥10 performed by an expert robotic surgeon, the authors reconfirmed the feasibility of RAPN for complex cases, showing short WIT, acceptable major complication rate and good long-term renal functional outcomes. Specifically, median operative time, EBL and WIT were 120 min, 150 mL and 16 min, respectively. Two intraoperative complications occurred (4.5%): one inferior vena cava injury and one bleeding from the renal bed, which were both managed robotically. Postoperative complications were observed in 10 cases (22.7%), of whom 4 (9.1%) were high Clavien grade, including two bleeds that required percutaneous embolization, one urinoma that resolved with ureteral stenting, and one bowel occlusion managed with laparoscopic adhesiolysis. Two patients (4.5%) had positive surgical margins and were managed expectantly with no radiological recurrence at a follow-up of 23 months. Interestingly, in this study the authors reported no decline in serum creatinine and eGFR 6 months after surgery [47].

With regard to RAPN in solitary kidney, RAPN is rarely used for tumour in solitary kidneys and only by expert robotic surgeons. In 2013, Hillyer et al. reported the results of 26 (2.9% of the whole cohort) patients with a solitary

kidney treated at five academic institutions from May 2007 to May 2012. The study showed that RAPN was a feasible treatment option in this specific population by offering reliable preservation of renal function, low surgical morbidity and early oncologic safety in the hands of experienced robotic surgeons. Specifically, the authors reported a median WIT of 17 min and only two intraoperative complications. Postoperative complication rate was 11.5%, and, at median follow-up of 6 months, postoperative eGFR did not decline significantly [48]. In 2013, Panumatrassamee et al. compared 52 LPN and 15 RAPN robotic ones performed in a single institution between June 2000 and April 2012 for tumours in solitary kidney [49]. The study showed that RAPN offers a significant benefit over LPN in terms of operative time, WIT and hospital stay. Conversely, no significant differences were found in terms of EBL, transfusions, complications, pathological results, margin status and postoperative renal function [49].

A minimally invasive PN in the setting of multifocal renal masses is challenging but can be performed in experienced hands. Both LPN and RAPN have been described. Although both procedures are feasible, patients must be appropriately informed about the risk of open conversion [50]. For synchronous, bilateral renal tumours that require intervention, the timing of surgery remains under debate. Surgical strategies can be concomitant, bilateral PN, staged PN with the larger/more complex side first or, conversely, staged PN with the smaller/less complex side first. Performing bilateral concomitant LPN or RAPN is difficult due to patient positioning changes and is often not feasible [50]. For staged LPN or RAPN, the strategy to start from more complex or less complex side is no different from open PN. In 2009, Boris et al. reported the results of initial experience with RAPN for multiple renal masses demonstrating the feasibility of this procedure. Specifically, a total of 24 tumours in nine patients were removed with robot assistance [51]. In 2013, Abreu et al. evaluated perioperative outcomes in a series of patients who underwent minimally invasive PN for multiple renal tumours. They performed a matched pair-analysis comparing 33 patients who underwent RAPN for multiple tumours with 33 who received the same treatment for a single tumour. EBL and WIT were similar in both groups. Conversely, median operative time and hospital stay were longer in the patients with multiple tumours. There were two conversions to laparoscopic RN per group. Overall, complications developed in 33 and 21% of the patients treated for multiple vs. single tumours. Median eGFR at discharge was similar in the two groups [52].

Very few reports are available in the literature concerning RAPN for treatment of a new or recurrent tumour in a kidney previously treated with PN. In 2008, Turna et al. reported the first experience with repeat LPN. They included in analysis 25 cases initially treated with open PN. WIT and EBL were 35.8 min and 215 mL, respectively. No intraoperative complications were reported, and postoperative complication rate was 12% [53]. Recently, Autorino et al. reported the results of the first series of repeat RAPN. They described the perioperative outcomes of nine patients previously treated with open, laparoscopic or robot-assisted PN. In three cases the surgeon performed an unclamping technique. In the remaining cases, WIT was 17.5 min. The EBL was 150 mL, and no intraoperative complications were reported. Postoperative complications were observed only in two cases [54].

Conclusions

The results of the available studies indicate that RAPN in the hands of expert surgeons is associated with excellent outcomes in terms of perioperative complications and functional results. RAPN may also be indicated in complex tumours, including hilar lesions, bilateral tumours, tumours in solitary kidney or tumours in kidneys previously treated with partial nephrectomy. Such special indications require the expertise of very experienced surgeons. The natural history of the small renal masses typically treated with RAPN as well as

the short-term follow-up available in the published studies due to the relatively recent development of the procedure prevent from drawing definitive conclusions on the oncological outcomes.

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Other Minimally Invasive Approaches (LESS and NOTES)

11

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Abbreviations

LESS	Laparo-endoscopic single-site surgery
MAGS	Magnet anchoring and guidance system
NOTES	Natural orifice transluminal endoscopic surgery
SAS	Single-access surgery
SILS	Single-incision laparoscopic surgery
SPA	Single-port access

Key Messages

- Both natural orifice transluminal endoscopic surgery (NOTES) and laparo-endoscopic single-site surgery (LESS) have been used in the management of small renal masses in various centres with comparable results.
- Difficulties of single-site surgery include instrument clashing, sword crossing and a limited range of movement.
- A variety of specific ports and instruments for single-site surgery are now commercially available.
- Given the technical challenges of single-site partial nephrectomy, it remains an experimental technique limited to specialist centres.

11.1 Introduction

With the development of laparoscopy, there has been a transition from multiple ports to single-port access. Laparo-endoscopic single-site surgery (LESS) is becoming an attractive for a variety of procedures. Furthermore, intra-abdominal procedures have been approached with a transluminal route (vagina, anus, urethra and mouth) leaving the patient without scars. Natural orifice transluminal endoscopic surgery (NOTES) and LESS are exciting new developments in the evolution of minimally invasive

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surgery. Both represent a natural progression of laparoscopic surgery with ever fewer and smaller incisions whilst also sharing common challenges. NOTES as a concept offers the potential for surgery without any transcutaneous abdominal incisions. LESS appears to offer a natural intermediate step towards a NOTES approach and may prove more practical in many applications.

These techniques share the common underlying premise, which has driven their development, that reduced transcutaneous access may benefit patients in terms of port-related complications, recovery time, pain and cosmesis [1]. Both NOTES and LESS have been used in the management of small renal masses in various centres with comparable results. Each approach will ultimately need to demonstrate its advantages in managing small renal masses over more traditional techniques in order to gain general acceptance.

11.2 Laparo-endoscopic Single-Site Surgery

11.2.1 Definition and Nomenclature

LESS represents any minimally invasive intra-abdominal surgical procedure performed through a single incision, utilizing conventional laparoscopic or newly emerging instruments. The nomenclature of laparoscopic surgery with single incision has been a source of confusion. Previous terms used in the literature have included SILS ("single-incision laparoscopic surgery"), SPA ("single-port access") SAS ("single-access surgery") amongst others. In an effort to reduce this confusion, it was proposed to decide on a single term that can be used internationally. "LESS" (laparo-endoscopic single-site surgery) was suggested by an interdisciplinary group of surgeons that formed a new organization called LESSCAR (laparo-endoscopic single-site consortium for assessment and research). It was decided that whether the surgery is performed via a single incision with multiple ports, a multichannel port or several small incisions grouped in one location, all such procedures should be considered equivalent to LESS [2].

11.2.2 History and Evolution

Hirano et al. reported the first urological single-incision surgery in 2005 [3]. They used a resectoscope and standard laparoscopic instruments to demonstrate the feasibility of a retroperitoneoscopic adrenalectomy. In 2007, Raman et al. reported the first LESS transumbilical nephrectomy [4]. Following an initial porcine feasibility model, three human nephrectomies were performed. Since then, a number of clinical series of urological procedures have been reported [5].

11.3 LESS Scopes, Instruments and Equipment

During its infancy, a major issue for LESS was the lack of appropriate equipment, hindering safe implementation of the technique. New multichannel single ports were required to safely introduce the instruments. Furthermore, conventional laparoscopic instruments led to instrument clashing, sword crossing and a very limited range of movement due to the lack of triangulation, resulting in significant difficulties for the operating surgeons [6]. Introduction of specially designed access ports as well as pre-bent and articulating instruments for LESS has helped resolving some of these difficulties and reducing operative time.

11.3.1 Access Devices

During the initial period, a number of commercial ports were developed of many of which are currently available including the SILS™ port (Covidien, Dublin, Ireland), which provides three channels 5 or 12 mm in diameter. GelPOINT™ (Applied Medical, Rancho Santa Margarita, CA) provides triangulation for the laparoscopic instruments through its rubber-sealing cap. The use of an Alexis retractor in its structural design allows the overextension of the incision and the enlargement of the working surface enabling the use of a home-made single-port platform [7]. The Quadport + ™ (Olympus, Tokyo, Japan) offers an extra port for entry and a wide variety of channel diameters (5, 10, 12 and 15 mm). All these

ports can be introduced by the modified Hasson method into the peritoneal cavity. Articulating, pre-bent and conventional laparoscopic instruments can be inserted through the GelPOINT, Triport+ and Quadport +, whereas the SILS port provides access only to articulating and conventional laparoscopic instruments.

Reusable ports such as the X-Cone™ and EndoCone™ (Karl Storz, Tuttlingen, Germany) have been introduced, offering a potentially more cost-effective solution. Recently, Intuitive Surgical developed a new set of single-site multichannel access port with four cannulae and an insufflation valve. One cannula holds an 8.5-mm robotic endoscope, two curved cannulae hold robotic instruments, and one 5-/10-mm cannula provides access for the bedside assistant. The curved cannulae are integral to the system, since their configuration allows triangulation of the instruments to the target anatomy. This triangulation is achieved by crossing the curved cannulae through the access port.

11.3.2 Instruments

Instruments such as Autonomy Laparo-Angle™ instruments (Cambridge-Endo, Framingham, MA) and Roticulator™ instruments (Covidien, Dublin, Ireland) provide seven degrees of freedom with 360° rotation around their axis by using an articulating mechanism that also allows deflection of the instrument's tip. However, the improved ergonomics comes at the expense of reduced joint forces necessary for secure knot tying and tissue traction [8]. In contrast, pre-bent instruments, such as the HIQ LS™ hand instruments (Olympus, Tokyo, Japan) and the S-portal™ series (Karl Storz, Tuttlingen, Germany), have fewer degrees of freedom but are reusable and more cost-effective. To compare standard laparoscopic and specific LESS instruments, mini-laparoscopic instruments have been used in LESS as alternatives to specifically designed LESS instruments. In fact, it was found that the mini-laparoscopic instruments facilitate the performance of LESS procedures, which would have been otherwise significantly more challenging despite the use of LESS equipment. Several instrument manufacturers produce mini-laparoscopic instruments with diameters ranging between 2.3 and 2.7 mm, such as the MiniLap™ series (Mini-Lap Technologies Inc., Dobbs Ferry, NY) and SLIMpac™ Mini-Laparoscopy System (Blue Endo, Lenexa, KS). The SPIDER™ Surgical System (TransEnterix, Durham, NC) is a combination of an access platform and laparoscopic instruments in one device. The design of this device avoids instrument crossing by providing two statics and two flexible working channels. Various LESS instruments and equipment are summarized in Table 11.1.

11.3.3 Optics

The development of articulating laparoscopes aimed to reduce the clashing with the other instruments. The EndoEye™ series (Olympus, Tokyo, Japan) and the EndoCAMeleon™ (Karl Storz, Tuttlingen, Germany) are both 10-mm laparoscopes with the sensory chip rotating within the tip of the instrument. The EndoCAMeleon's design avoids a flexible shaft of the laparoscope, with a possible advantage in the durability of the instrument. A unique innovation introduced by Park et al. [9] was the magnet anchoring and guidance system (MAGS). The use of the MAGS camera in LESS procedures has been proven to offer an improvement in the ergonomics to the surgeon. The system is composed of an intra-abdominal camera that can be manipulated via an extracorporeal magnetic handle. The instruments are anchored with the use of external magnetic anchors. The light source for the procedure is based on the integration of optic fibers in the inserted trocar.

11.4 Laparo-endoscopic Single-Site Radical Nephrectomy

The largest multi-institutional LESS series, including 1076 cases, was presented by Kaouk et al. in 2011 [10]. The majority of the cases were nephrectomies, and robotic LESS (R-LESS) cases represented 13% of the population. In this large series, which included the experience of 18

Table 11.1 Laparo-endoscopic single-site surgery: access devices, instruments and optics

Category	Name	Features
Access devices	GelPOINT (Applied Medical)	Three components: GelSeal providing PseudoAbdomen platform; Alexis wound retractor; self-retaining trocars. Larger outer working profile for enhanced triangulation; adapts to size of incision and abdominal wall thickness; fragile
	SILS port (Covidien)	Flexible platform; up to three individual ports and instruments. Easy exchange of different sized ports; difficult suturing for robotic LESS; difficult to use with large abdominal wall
	Triport (Olympus)	Flexible multichannel valve; up to three instruments, covered with an elastomer; Hassan introduction Adapts to size of incision and abdominal wall thickness; fragile when using 12-mm instruments; lubrication required; constrictive outer ring
	Quadport (Olympus)	Flexible multichannel valve; up to four usable ports; instruments covered with an elastomer
	SPIDER Surgical System (TransEnterix)	The SPIDER Surgical System is composed of two primary assemblies: a platform access device and a stabilizer with a bed clamp. It includes an insertion trocar covered by a retractable sheath and nose cone and four working channels
	AirSeal (SurgiQuest)	No physical seal, AirSeal maintains pneumoperitoneum by creating an air vortex. Multiple instruments to fit through one large opening in the trocar.
	OCTO-Port (Dalim SurgNet)	The OCTO-Port consists of a lower base plate that sits under the skin edge in the peritoneum, an external disc with self-retractor, and a transparent silicone cover with three or four channels
	da Vinci single-site port (Intuitive Surgical)	The five-lumen port provides access for two single-site instruments: 8.5-mm 3D HD endoscope, 5-/10-mm accessory port and insufflation adaptor
Instruments	Roticulator (Covidien)	5-mm dissector, scissors, grasper
	RealHand instruments (Novare Surgical Systems)	Hand-held scissors, dissector, needle-holder, hook which allow for 360° reticulation mimicking the hand's movement
	Autonomy Laparo-Angle instruments (Cambridge Endoscopic Devices)	360° plane of movement and can be locked. Bulky handle
	S-PORTAL: series (Karl Storz)	Rigid instruments, preshaped, reusable
	Pre-bent	Reusable preshaped curved instruments
Optics	IDEAL EYES (Stryker)	Over 100° of flexion in all directions, 10-mm articulating scope, integrated light cable
	EndoEYE LTF VP (Olympus)	Articulating 5-/10-mm 0° digital scope with 100° angulation, skilled assistance required

institutions, the conversion rate to standard laparoscopy was 20.8%, and only 1% of the overall procedures required conversion to open surgery. The authors suggested that LESS is a safe approach in experienced hands with strict patient selection criteria. Whilst the majority of the surgeons performed a transperitoneal procedure for the nephrectomies, Dong et al. [11] used a retroperitoneal approach with similar safety results and outcomes using a home-made access device. Moreover, Park et al. [12] studied the learning curve of the LESS radical nephrectomy concluding that it is short for an experienced laparoscopic surgeon. The mobilization of the kidney was considered by the authors as the most difficult part to perform. There are several further studies in the literature showing the feasibility and the similar outcomes of LESS radical nephrectomy, in

comparison with the conventional laparoscopic nephrectomy [13–16].

11.5 Laparo-endoscopic Single-Site Partial Nephrectomy

Several studies have shown the feasibility of the LESS partial nephrectomy and also the feasibility and the satisfactory outcomes of the R-LESS partial nephrectomy. Perioperative details of the partial nephrectomy studies are shown in Table 11.2. Greco et al. [17] presented an analysis of 190 patients undergoing partial nephrectomy in 11 institutions. The authors found that higher PADUA (Preoperative Aspects and Dimensions Used for an Anatomical) scores were associated with higher the rate of complications. The use of the robotic platform resulted in a reduction in complication rates. The major limitations of the study were the retrospective design and differing selection criteria amongst the 11 institutions. Nonetheless, the authors suggested that LESS partial nephrectomy is safe in experienced hands. They also stated that patients with low PADUA scores should be preferable candidates for the LESS approach. Moreover, the use of Robotic-LESS (R-LESS) seemed to decrease even further the rate of postoperative complications. LESS partial nephrectomy represents the most demanding technique of upper urinary tract surgery [18], but it offers a feasible option for small renal masses that do not need clamping of the hilum or renorrhaphy.

11.6 Drawbacks of LESS

1. Instrument crowding: The close proximity of parallel instruments results in crowding. Clashing of instruments could be avoided by using pre-bent, articulated and instruments of various length (i.e. obese and paediatric equipment). Moreover, recently developed laparoscopes offer a streamlined profile compared to the standard laparoscopic light cable.
2. Triangulation: Instrument triangulation allows proper tissue retraction. Placing several parallel instruments makes triangulation more difficult.
3. Retraction: Retraction force is decreased with a single-site platform.

11.7 Natural Orifice Transluminal Endoscopic Surgery

11.7.1 Definitions and Nomenclature

The terminology of natural orifice transluminal endoscopic surgery (NOTES) was introduced by the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR), a joint

Table 11.2 Laparo-endoscopic single-site surgery (LESS) series for renal mass

Study	Year of publication	No. of cases	Mean operative time (min)	Mean estimated blood loss(cc)	Conversion rate (%)	Complications (*n*)
Aron [19]	2008	5 LESS-PN	270	150	20%	Postoperative haemorrhage and pulmonary embolism (1)
Kaouk [20]	2009	5 LESS-PN	160	420	20%	0
Stolzenburg [21]	2009	10 RN	146.4	202	0%	Transfusion (1)
Bazzi et al. [13]	2012	17 LESS-PN	176.2	170.6	11.7%	Clavien class IIIa (3) Clavien class II (2)
Greco et al. [17]	2013	119 LESS-PN 71 R-LESS PN	170	150	7.8%	28 (14.7%)
Tiu et al. [22].	2013	39 R-LESS PN	185	150	2.5%	Transfusion (5) Urine leakage (1)

initiative supported by the American Society for Gastrointestinal Endoscopy (ASGE) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) [23]. The primary aim of NOTES involves puncture of one of the naturally occurring orifices (e.g. vagina, urinary bladder, stomach, rectum) to access the abdominal cavity and perform intra-abdominal surgery. The advantages of NOTES include further reduction in the invasiveness of the surgical procedure with improved cosmesis even compared with LESS.

The use of a transabdominal port has not been considered as pure NOTES; however, it is regarded as a part of the development of this technique. Thus, the NOTES performed with combination of natural orifices, but with an additional transabdominal port, was defined as "hybrid" NOTES [2].

11.7.2 History and Evolution

Natural orifices include the vagina, urethra, oral cavity and rectum. Urologists have used the urethra to access the bladder, ureter and kidneys, whilst general surgeons and gastroenterologists have used both the oral cavity and the rectum for treatment of diseases of the alimentary tract. Gynaecologists have used the vagina for access to the uterus and for the culdoscopy. The first "hybrid" NOTES nephrectomy in porcine model was reported by Gettman et al. in 2002 [24]. Pure NOTES was first reported in 2004 by Kalloo et al. who performed transgastric peritoneoscopy and liver biopsies [25]. However, the upper gastrointestinal route for NOTES showed several drawbacks with difficult orientation and peritoneal contamination. These results gave way to the next generation of new access routes in the lower abdomen. Lima et al. established an atraumatic method to create a transvesical port for peritoneoscopy [26], and Fong et al. developed the transcolonic access in a porcine model [27]. The first pure NOTES of simple nephrectomy in a human was reported by Kaouk et al. [28]. Table 11.3 outlines the various routes for performing NOTES.

Table 11.3 Advantages and disadvantages according to transluminal approach

Transluminal approach	Characteristics
Transgastric	Advantages: Safe and well-known approach Disadvantages: Difficulties in spatial orientation, optimal closure technique and endoscopic retroflection for upper abdominal procedures
Transcolonic	Advantages: Offer easy access to multiple targets, retroperitoneum and easy visualization of upper abdominal organs. Colon compliance could tolerate larger instrument and specimen retrieval Disadvantages: High mortality of an incomplete closure of the colostomy site and subsequent peritonitis
Transvesical	Advantages: The urinary tract is normally sterile with a reduced risk of infection and peritoneal contamination. Cystotomy sites can be managed conservatively with catheter drainage Disadvantages: Relatively narrow diameter of urethra can limit introduction of instruments
Transvaginal	Advantages: Readily secure closure offered by standard surgical technique Disadvantages: Postoperative infection, visceral lesions and other long-term potential problems (e.g. dyspareunia, infertility)

11.8 Transluminal Approaches and Procedures

11.8.1 Principle of Surgical Steps in NOTES

1. Natural orifice is accessed through a natural orifice with a multichannel scope.
2. Incision through the orifice wall.
3. Placement of a wire into the abdominal cavity using a modified Seldinger technique.
4. Dilation balloon is used to obtain a suitable access tract.
5. Placement of a guide tube, catheter and CO_2 insufflation.

6. Scope is advanced into peritoneal cavity.
7. Performance of the diagnostic/operative procedure.
8. Closure of viscerotomy site.

11.8.2 Transgastric

After the endoscope is advanced into the stomach, the anterior stomach wall is punctured, a guide wire is advanced, a sphincterotome is inserted, and a gastric incision is performed. Gastrotomy closure is performed with suturing device or endoclips. NOTES procedures through an isolated transgastric route faced several limitations including the need for retroflexion of the endoscope for upper abdominal procedures, contamination of the peritoneal cavity and complex endoscopic closure of the gastrotomy. In attempt to overcome these limitations, several solutions have been proposed such as construction of more rigid transgastric platforms. Gastrotomy closure has become one of the key areas in NOTES research and development.

11.8.3 Transcolonic

A transcolonic access has the advantage of allowing larger-sized scopes with the rectum tolerating large instruments. However, this access remains a high-risk procedure, given the high bacterial load of the colon and potential for infection through introduction of faecal material into the peritoneum. The site of access is 15–20 cm from the anus. A drain is inserted into the abdominal cavity after intraperitoneal instillation of a decontaminating solution. Techniques for closure include endoscopic clips and stapling devices.

11.8.4 Transvaginal

Gynaecologists have been using a transvaginal approach for open surgery for many years. This orifice is very promising as a conduit for insertion of endoscopic instruments and cameras, given the relative ease of access. An advantage of the vagina for extirpative procedures is potential for using the colpotomy for specimen extraction, for example, a kidney specimen [24].

The colpotomy is typically closed easily under direct vision with little morbidity or discomfort [29]. An obvious disadvantage is its limited applicability to 50% of the population [30]. There also remain concerns about dyspareunia and leakage.

11.8.5 Transvesical

A significant advantage of a transvesical access is the sterility of urine [31]. Early descriptions of transvesical access have included use of a ureteroscope through a 5.5-mm transvesical port in a porcine model by Lima et al. The use of such a small scope does not necessarily require closure in their experience [26].

However, safe and reliable closure of a vesicostomy will need to be established for larger bladder defects. A flexible injection needle is advanced through a cystoscope to perforate the bladder dome. A balloon dilator is then passed over a guide wire.

11.9 NOTES Scopes, Instruments and Equipment

NOTES requires the equipment to allow retraction, cutting, retrieval of specimens, tissue approximation and closure of the access site defect. Endoscopic devices must be smaller than laparoscopic instruments. Articulating endoscopic instruments are also important tool in NOTES. Manipulation of tissues can be performed with various grasping devices such as endoscopic forceps. An early prototype described in the literature is the Eagle Claw (Olympus, Tokyo, Japan). A flexible stapling device for NOTES procedures is the iNOLC (intelligent Natural Orifice Linear Cutter, Power Medical Interventions, Langhorne, PA). Endoscopic clips have been described for closure of gastrotomies [32]. Some more sophisticated clips have the ability to rotate and open and close multiple

times, e.g. the Resolution Clip (Boston Scientific, Natick, MA).

Given the limitations of current NOTES endoscopic instrument, such as reduced traction–counter traction and limited force, the use of magnetically anchored and guided system (MAGS) instrumentation and the development of multitasking endoscopic platforms have been proposed [23]. A flexible articulating laparoscopic grasper improved triangulation after positioning the MAGS instruments. The hilum was controlled using an extra-long endoscopic stapling device. Recent innovations in NOTES platforms include the TransPort (USGI Medical San Clemente, CA, USA), Cobra (USGI Medical, San Clemente, CA, USA), Endo-SAMURAI (Olympus Corp, Tokyo Japan) and the Direct Drive Endoscopic System (DDES) (Boston Scientific, Natick, MA, USA). The multitasking platforms, such as TransPort and Cobra, have a common flexible endoscopic design. The operator interface is similar to conventional operating gastrointestinal endoscopes. All have independent steering mechanisms for the scope tip after the endoscope is locked in position at the target. The TransPort and Cobra utilize ShapeLock technology (USGI Medical, San Clemente, CA, USA). The Cobra uses three independent arms at the tip of the ShapeLock shaft to enhance instrument triangulation, with the optics elevated above the plane of the operating instruments (Table 11.4).

Table 11.4 Natural orifice transluminal endoscopic surgery platforms

NOTES platform	Characteristics
Cobra ™ (USGI Medical, San Clemente, CA, USA)	ShapeLock-based shaft to solve the triangulation with three independently moving arms
TransPort™ Multi-lumen Operating Platform (USGI Medical, San Clemente, CA, USA)	Provide stable platform by using ShapeLock technology which inserted in flexible state and locked into a rigid configuration
Anubis™ (Karl Storz, Tuttlingen, Germany)	Allows distal triangulation with at least three working instruments and controlled insufflation
Cobra ™ (USGI Medical, San Clemente, CA, USA)	Instrument has control handles which transmits hand motion to the instruments tips with five degree of freedom

11.10 Natural Orifice Transluminal Endoscopic Nephrectomy

Given the novel technology of NOTES, experimental studies using porcine model were reported initially. In 2002, Gettman et al. described the first porcine transvaginal laparoscopic nephrectomy [24]. A single 5-mm transabdominal additional trocar for the laparoscope was required to facilitate visualization. However, the procedure was compromised by poorly adapted instrumentation and was not yet ready for human study. To develop pure NOTES nephrectomy for clinical application, Aron et al. experiment on a human cadaver model using a rigid transvaginal platform [33]. They used a multichannel R-Port placed into the umbilicus, a Quadport into the vagina, straight and articulating laparoscopic instruments and a rigid 10-mm, 30° laparoscope. Three nephrectomies were successfully performed. In the first two cadavers, transient umbilical assistance was necessary towards the end of the procedure to release posterosuperior attachments between the upper pole kidney and the diaphragm. In the final case, the entire dissection was completed with a transvaginal flexible gastroscope, without any transabdominal assistance. This study provided some helpful tips for transvaginal NOTES nephrectomy: the cephalad aspect of the hilum and the upper pole attachments are problematic areas for transvaginal dissection, and extra-long laparoscopic instruments and flexible instruments can be useful in NOTES nephrectomy.

However, flexible NOTES instruments have been criticized as providing inadequate retraction with severe limitations in haemostatic devices. Further minimizing the use of accessory transabdominal ports, in 2009 Kaouk and colleagues successfully performed the world's first human transvaginal NOTES nephrectomy on a 57-year-old woman with a non-functioning right kidney

[34]. The procedure was successfully completed, with all the operative steps performed transvaginally. Pelvic adhesions from a prior hysterectomy necessitated the use of only one 5-mm umbilical port during vaginal port placement and for retraction of the ascending colon during division of the renal hilum. No intraoperative complications occurred using a standard flexible video gastroscope. Two 10-mm standard trocars and one 5-mm standard trocar were placed across the GelPort through which a 5-mm deflecting laparoscope (Olympus Surgical, Orangeburg, NJ, USA) and a 45-cm articulating graspers and scissors (Novare Surgical, Cupertino, CA, USA) were placed. The first stage of the NOTES nephrectomy was to develop the plane between the retroperitoneum and the mesentery of the colon. After exposing the hilum, an endovascular stapler was fired across the renal vein and renal artery. The remaining posterior and upper pole attachments were taken down using an extra-long (65 cm) monopolar J-hook with care taken to spare the adrenal gland. The kidney was placed into a retrieval bag and brought out through the existing vaginal incision with no perioperative complication.

11.11 Natural Orifice Transluminal Endoscopic Partial Nephrectomy and Nephron-Sparing Surgery

Nephron-sparing surgery using a NOTES technique remains an experimental procedure which has only been tested in animal study. A NOTES transgastric partial nephrectomy was performed by Boylu et al. in 2009 to evaluate the feasibility of NOTES partial nephrectomy without hilar clamping in a porcine model [35]. The gastroscope was introduced through the esophagus, and a 2-cm gastrotomy was performed using an electrocautery needle at the junction of the fundus and the proximal body. After incision of Gerota's fascia, the left kidney's upper pole was excised using the thulium laser with an off clamp technique. An endoscopic wire loop was used to entrap and extract the specimen into the stomach. The gastroscope was subsequently withdrawn with the intact specimen. After haemostasis, metal clips were applied endoscopically to close the gastrotomy.

Crouzet et al. reported their experience with NOTES renal cryoablation in a porcine model [36]. The procedure was performed either with a transvaginal or transgastric approach. Pneumoperitoneum was first obtained using a Veress needle. The kidney was approached with a video gastroscope. The stomach wall was punctured using a needle knife, a guidewire was passed into the abdominal cavity, and the access dilatation was performed using a controlled radial expansion balloon. Under direct endoscopic vision, a cryoablation probe was introduced percutaneously into the anterior upper pole of the kidney. Overall, four procedures were performed successfully, with no intraoperative complications and no need for additional laparoscopic ports or open conversions. Stomach closure was tested and found to be watertight. Given the technical difficulty in performing NOTES in nephron-sparing surgery, further animal and cadaveric study is needed for human application.

Conclusion

Although NOTES may prove to be the future frontier of minimally invasive surgery, it currently remains an experimental approach in small renal mass surgery. Given the rapid pace of innovation to date, we anticipate further developments of instruments and devices that are expected to define its area of future application.

Additionally, LESS has proved to be immediately applicable in the clinical field, being safe and feasible in the hands of experienced laparoscopic surgeons in well-selected patients. Promising early outcomes, the benefits of LESS are reported and importance in evaluating the role of these approaches is needed to critically assess new technologies and ensure at least equivalency of these techniques for safety of small renal mass patient, including oncologic principles and efficacy.

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12 Training and Simulation in the Management of Small Renal Masses

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Abbreviations

LPN	Laparoscopic partial nephrectomy
OR	Operating room
RAPN	Robot-assisted partial nephrectomy
VR	Virtual reality

Key Messages

1. Modern concepts such as fellowships, telementoring and e-learning can enhance workplace-based training.
2. There are several highly validated robotic VR simulators and basic laparoscopic skills curricula, which should form the first step in LPN and RAPN training.
3. Procedure-specific dry lab and VR trainers are very limited in number and low in evidence base. Thus, simulation-based training should be focused on basic skills acquisition.
4. Human cadavers and live animal models, where available, can be utilised to refine skills as masterclasses at the advanced stage of training.
5. Non-technical skills training should also take place within training using high fidelity or simulation or full immersion simulation.

12.1 Introduction

The advance of medical technology, over the last decade, has revolutionised surgical practice. This has undoubtedly had a major effect upon all surgical specialties including urology. The surgical methods for treatment of kidney, bladder and

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prostatic disease have radically evolved from open wound surgery to a much more minimally invasive approach.

These changes in surgical practice, coupled with the introduction of European working time directives, greater patient expectations and financial constraints in the NHS and other healthcare organisations, have raised fundamental questions on postgraduate surgical training. The concern that surgical residents are not receiving adequate training is becoming greater. Furthermore, the introduction of new procedures has raised concerns about patient safety. A prime example of such development is the management of small renal masses. The widespread utilisation of procedures such as laparoscopic partial nephrectomy (LPN) and robot-assisted partial nephrectomy (RAPN) has made it essential to combine work-based surgical training with simulation, in order to acquire skills outside the operating room (OR) without compromising patient safety.

However, before any simulators can be used for training and assessment, it must undergo an initial internal assessment across a variety of parameters (Fig. 12.1) [1, 2]. This chapter will outline the current concepts in surgical training, with a focus to training for surgical management of small renal masses, and evaluate the evidence base for such training methods.

12.2 Workplace-Based Training

12.2.1 Observership

The practice of observing another surgeon perform a procedure has long been the initial step in surgical training, since the classic Halstedian method of training has been utilised [3]. Via observation of expert surgeons, trainees can familiarise themselves with the basic principles of surgery, build procedural knowledge and also come to appreciate the difference between open surgery and minimally invasive surgical modalities such as laparoscopy and robotics [4]. With the additional benefit of being able to ask questions during procedure to fill gaps in knowledge, observership has been seen as a vital first step in the development of successful training programmes [5].

Despite this training method being utilised widely, there are limitations to its use. There is a limitation in the development of technical skills with true observership which may therefore require additional training methods, such as simulation-based training [6]. Additionally, the increasing use of minimally invasive techniques causes further problems, in particular robotic procedures, where the patient-side assistant is unable to directly view the precise hand movements of the surgeon. Finally, within the literature there is additionally a distinct lack of evidence to demonstrate improved outcomes to

Face Validity – Opinions, including of non-experts, regarding the realism of the simulator

Content Validity – Opinions of experts about the simulator and its appropriateness for training

Construct Validity

- Within one group – Ability of the simulator to assess and differentiate between the level of experience of an individual or group measured over time
- Between groups – Ability of the simulator to distinguish between different levels of experience

Concurrent Validity – Comparison of the new model against the older and gold standard, usually by OSATS

Predictive Validity – Correlation of performance with operating room performance, usually measured by OSATS

Fig. 12.1 Definitions of validity, based on definitions by McDougall [1] and van Nortwick et al. [2]. *OSATS* objective structured assessment of technical skills

patients when utilising this training method, largely due to the difficulties in assessing the effectiveness of pure observership in improved operative performance. Despite these limitations, there has not been a lack of recommendation in its use within robotic curricula developed by the European Association of Urology and the British Association of Urological Surgeons and certainly remains an important initial component in training novice surgeons in renal masses [7, 8].

12.2.2 e-Learning

As access to the Internet at all times increases, along with the increasing demand for more flexible training methods, e-learning has become increasingly used in urology training. It may be defined as the use of the Internet and multimedia technology to deliver training and aid learning [9]. It provides a training tool which cannot only be accessed at a trainee's convenience, but additionally can be updated along with most recent guidelines. There is an extensive evidence base surrounding its benefit in a variety of surgical specialties, and it can even be aimed at teaching surgical skills [10]. However, similarly to observership, whilst surgical techniques and steps can be demonstrated, it cannot develop technical skills as a stand-alone modality of training. Hence, it has been recommended as useful in the initial phase of training, along with observership to develop procedural knowledge [7]. There are already established online modules addressing renal carcinomas and masses, developed by the European Association of Urology and the American Association of Urology, which deliver this more novel training method [11, 12].

12.2.3 Mentorship

Mentorship within modern surgical education is defined as the "off-line help by one person to another, making significant transitions in knowledge, work or thinking" [13]. It is an old and crucial practice and has played a significant part in training surgeons since the Halstedian apprenticeship model was introduced in 1889 [14]. The expectation is that a mentor will assist trainees in developing not only their technical skills but additionally the non-technical skills required to reach competence in their practice. However, mentors may also benefit their mentees in other ways such as increasing their social network for career progression. It is important that trainees are able to develop constructive relationships with their mentors [15].

In traditional open and laparoscopic surgery mentorship provides a safe and effective training method. With both surgeons sharing the same field of view, it is easy for an expert to intervene at any stage, thereby reducing the risk of complications and compromise in patient safety during the initial learning period. However, this has only recently become possible in robotic surgery due to the limitation of the design of previous consoles [16]. However, with the third-generation da Vinci© Robot offering dual consoles, there is now the possibility to increase the use of mentorship during robotic procedures.

As we understand more about the effect of mentorship on surgical training, the role of the mentor is being increasingly understood. It is important they initially possess the experience and skills necessary to teach the procedure [17]. Additionally, it is increasingly understood that the ability to share your expertise, required during effective mentorship, is not always an innate trait and there is a need to train mentors for effective delivery of training [18]. Finally, it is recognised that there is a need for mentorship programmes to be structured, with clear learning objective and training pathways preceding a formal sign-off process [19].

Structured mentorship programmes have been demonstrated to be useful within nephrectomy training. Cook and colleagues developed a structured mentorship programme within paediatric urology trainees for performing nephrectomies, demonstrating it to be an effective and safe method of training novice surgeons [20]. Additionally, mentorship has been demonstrated to be a useful training tool not only for

trainees, but additionally for new consultants looking to expand practice to include nephrectomies, as demonstrated by the mentorship programme setup by BAUS in 1999 [21]. A study has demonstrated that mentorship from visiting experts has provided a good training tool for 39 consultants, with 29 of these being able to develop an independent practice and without any major complications noted within the study period.

12.2.4 Fellowships

Structured mentorship programmes have often been delivered via formal fellowship or mini-fellowship programmes. These programmes are offered at institutions across the globe and are aimed at providing focused exposure to a specific area of interest, often in the later stages of a trainee's development [22]. Interestingly a trainee and trainer survey has demonstrated that many believe this not to be an essential process for independent practice of nephrectomies [23]. However, there is evidence to demonstrate that those who attended mini-fellowship and longer fellowship programmes have a good educational impact in laparoscopic renal surgery and produce outcomes similar to experienced surgeons [24, 25]. Therefore, whilst not essential parts within training, fellowships certainly provide an important training modality.

12.2.5 Telementoring

An interesting expansion of the traditional mentorship model has arisen via telementoring. The first video teleconference was conducted in 1962, when DeBakey demonstrated open-heart surgery, a pioneering step in establishing the field of telemedicine [26]. With the rise of laparoscopic surgery, this became easier, and Cubano et al. [27] performed a number of general surgical laparoscopic procedures aboard a naval vessel, via an intercontinental telementoring system, identifying a useful opportunity to improve patient care by seeking instant expertise. Telementoring or distance mentoring is surgical mentoring at a distance, whereby the mentor and mentee are at separate locations [28], where the distant mentor may be a senior colleague or a peer [15].

Telementoring has been identified as demonstrating educational benefit and having a positive effect on surgical education [29, 30]. Whilst there is no direct evidence for its use in the training of small renal masses, its use in urology is proven. There is evidence to demonstrate it produces a similar learning curve to traditional mentoring techniques within robotic radical prostatectomy [31] and aids independent practice within living donor nephrectomy [32]. However, as this training method expands with the rise of minimally invasive surgery, it is important to consider some of the legal and ethical considerations it raises. With issues regarding recognition of qualifications in different countries, patient confidentiality and legal liability of surgical errors, it is important to utilise telementoring in the context of strict institutional guidelines [33].

12.2.6 Modular Training

Modular training describes the process of learning a procedure in steps with differing levels of difficulty, whereby a trainee would not perform the entire procedure initially, however develops progressively the skills to do by learning steps of increasing difficulty [34]. This provides a structured training method where independent performance of all the steps and eventually the whole procedure is the final objective. Modular training is shown to be an effective and safe method of training both trainees and consultants to perform laparoscopic nephrectomies [35, 36]. However, there are still issues with the definition of what the models of differing difficulty are in, and progression between different models is still a largely subjective practice [37]. Modular assessment tools have been developed for robotic radical prostatectomy; however, unfortunately there is currently no such tool available for the training of renal masses [38].

12.2.7 Proctorship

Surgical proctorship is a training tool that may utilise various elements mentioned previously to develop trainees. It is defined as the knowledge and skills assessment of a trainee by an expert, who is often from a different institution, who is therefore responsible for supervising them in initial phase of the learning curve of a procedure [39]. The process may be initiated by the trainee visiting the proctor and observing various procedures. Subsequently, the proctor is required to visit the trainee's hospital to assist them in operations and give the trainee varying levels of responsibility in accordance to their level of skills and knowledge. As can be imagined, this process can be costly and time consuming. However, the increasing use of telementoring and the ease of recording videos of procedures may overcome these hurdles. However, despite its current limitations, the process is demonstrated to provide good training outcomes in both urological and general surgical procedures [40, 41]. It provides a structured approach to ensure progression along the learning curve whilst still ensuring patient safety is maintained [42] and thus provides another useful training modality.

12.3 Simulation-Based Training

Over the past two decades, surgical simulation has developed at a rapid pace, becoming an established method of training and assessment. Alongside suitable fellowships, it has been shown to improve trainee performance in the operating room [43]. Surgical management of small renal masses is achieved in the form of LPN and RAPN. However, both have been associated with a steep learning curve, and thus, simulation has been widely adopted to overcome these challenges [44].

12.3.1 Basic Laparoscopic Skills Acquisition

In contrast to procedure-specific models, there are an overwhelming number of simulators and/or models for acquiring basic laparoscopic skills in the form of virtual reality (VR) and box trainers [45, 46]. Great efforts have been spent to develop and/or optimise laparoscopic skills training using box trainers. A prime example of this is the highly validated Fundamentals of Laparoscopic Surgery (FLS©) skills curriculum. Based on this, several urology-specific curricula have also been developed including the Program for Laparoscopic Urological Skills (PLUS) [47, 48], the Basic Laparoscopic Urologic Surgery (BLUS©) skills [49] and the European Basic Laparoscopic Urological Skills (E-BLUS) [50]. Sweet et al. [49] demonstrated face, content and construct validity and acceptability of BLUS amongst 116 participants consisting of practicing urologists, fellows, residents and novices. Similarly, the PLUS curriculum has also demonstrated face, content and construct validity [47] and established itself as reliable method of assessment [48].

12.3.2 Laparoscopic VR Simulators for LPN

VR Simulation in laparoscopic procedural training is limited by the lack of validation studies on commercially available platforms and the lack of availability of the only validated simulator for laparoscopic radical nephrectomy, the Procedicus MIST (Mentice, Gothenburg, Sweden). The platform has demonstrated face, content and construct validity amongst experts, trainees and novices in two similar studies [51, 52]. However, Wijn et al. [53] reported failure of the trainer to demonstrate construct validity in a cohort relatively higher in number ($n = 64$). The model does not appear to be commercially available.

The LAP Mentor (Simbionix, Lod, Israel) and LapSim (Surgical Science, Gothenburg, Sweden) are both commercially available VR simulators that include basic camera and laparoscopic skills as well as procedure-specific modules, one being nephrectomy. Although the simulators have been validated for basic skills, the nephrectomy modules are yet to be scientifically evaluated.

12.3.3 Basic Robotic Skills Acquisition

Using the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) for training can allow trainees to familiarise with general instrument operation, docking, gain experience in operating the console and work without tactile feedback. It can also be utilised for basic skills practice such as suturing, precision cutting and ring-peg transfer, which are required to progress to more complex tasks, in a risk-free environment. However, such training necessitates a functional robot, and their current expense limits their widespread use for training. Fortunately, robot-assisted surgery has been well suited to VR simulation, and currently, there are a number of available simulators:

1. Robotic Surgical Simulator (RoSS; Simulated Surgical Systems, Buffalo, NY, USA)
2. dV-Trainer™ (Mimic Technologies Inc., Seattle, WA, USA)
3. SimSurgery Educational Platform (SEP) Robot™ (SimSurgery®, Oslo, Norway)
4. *da Vinci* Skills Simulator (dVSS; Intuitive Surgical, Sunnyvale, CA, USA)
5. Promis (CAE Healthcare, Saint-Laurent, Quebec, Canada)
6. RobotiX Mentor (Simbionix, Cleveland, OH, USA)

Although majority of the simulators have demonstrated validity for basic skills acquisition, the most comprehensive evaluation has been performed on the dV-Trainer followed by the dVSS, both of which utilise the same software by Mimic Technologies. Amongst the validated simulators, the SEP Robot has not demonstrated educational impact due to its differences with the da Vinci System [52, 54, 55].

12.3.4 Robotic Simulators for RAPN

The only procedure-specific training available is on the dv-Trainer. The Maestro Augmented Reality system (Mimic Technologies), released in 2014, provides procedure-specific training, through the manipulation of a 3D anatomical video. The partial nephrectomy module has demonstrated face, content, construct and concurrent validity, amongst 42 participants [56].

12.3.5 Synthetic (Bench) Models

Surgical simulation may be performed using a range of physical models made from latex, rubber or plastic, which are created to represent various organs and their associated pathological states. This can be used by surgeons to perform a number of specific procedures with the benefit of recreating the tangible sensations of the real surgical environment. Synthetic models, within laparoscopic box trainers or use with a training robot, may be useful for improving hand–eye coordination as well as the technical motor skills required for tasks such as suturing, cutting and knot-tying. Hence, they can be especially useful in training certain parts of full operations. However, replacement of the models is required following each use.

A limited number of dry lab models have been developed and validated for use with the da Vinci Surgical System. Ramos et al. [57] validated three dry lab models "reverse engineered" from the Mimic Msim VR software. The three basic skills models demonstrated face, content and construct validity. SIMPLE (Simulated Inanimate Model for Physical Learning Experience) is a procedure-specific training model for RAPN. Using a 3D printed replica kidney and tumour, it provides simulation to perform the steps of RAPN. Face, content and construct validity was demonstrated using objective parameters of ischaemia time, blood loss, positive margins and estimated blood loss [58]. However, a small cohort of three experts, three intermediates and two novices means further validation is required. Patient 3D printed models have also been created to allow simulation prior to surgery [59] but require educational evaluation.

12.3.6 Animal Models

Animal models offer many advantages over bench models, such as respiratory movement and

authentic haptic feedback [60]. However, despite having a higher degree of face validity, their use as a training method is often limited by their availability. Hence preference is given to surgeons requiring advanced training in a high-fidelity environment. Although assessment within the animal laboratory is much more cost effective and reproducible when compared to human cadavers, their use is further limited as a result of licencing and ethical issues [61]. Therefore trainees often travel to certain countries to receive wet-lab training. Both ex vivo and in vivo animal models have been used for robotic training. Unfortunately, few studies have documented their educational impact.

Amongst various proposed animal models, the rabbit model of training has been validated for improving basic surgical skills including suturing, knot-tying and dissection, all essential in performing LPN and RAPN [62]. Xu et al. [63] used animal models within laparoscopic box trainers to simulate partial nephrectomy and pyeloplasty. The authors demonstrated improvement and construct validity amongst 33 trainees but failed to describe the details of which animal models were used.

Molinas et al. [64] report the use of live rabbits to train ten medical students and ten gynaecologists to perform laparoscopic radical nephrectomy. Each participant performed 20 procedures, at the end of which time and rates of complications significantly reduced. Furthermore, gynaecologists achieved shorter operating times than students for the first last procedures, whilst severe complications were more frequent in the student group. Similarly, Hung et al. [65] described a tissue model for RAPN training consisting of a porcine kidney and a polystyrene ball to mimic a tumour. Face, content and concurrent validity was established amongst 46 participants consisting of 24 novices, 9 intermediates and 13 experts. Further analysis during a larger trial supported its concurrent validity [66].

12.3.7 Human Cadavers

Surgical training using human cadavers has been a crucial part of training for minimally invasive surgery [67]. Many surgical training courses have integrated this modality as it has the added benefit of replicating human anatomy. Such training allows surgeons to perform and practice more complex tasks after reaching a level of proficiency in basic surgical skills. However, training should always be accompanied by active instruction and feedback by an expert [44]. However, the evidence behind their use is limited by studies of low participant size and/or quality, which are often survey studies. It is generally assumed that Thiel-embalmed cadavers have a higher sense of realism in contrast to fresh frozen cadavers, but this is yet to be proven [44].

As with animal models, there has been sparse validation of the effectiveness of cadaveric training in robotic surgical training. Raison et al. [68] reported the use of fresh frozen cadavers for multiple robotic procedures, including RAPN, and demonstrated face, content and construct validity in a study of 16 intermediate and 4 expert participants. Ahmed et al. [69] described the British Association of Urological Surgeons (BAUS) Human Cadaver Training Programme. The authors report a comprehensive curriculum utilising fresh frozen cadavers where open emergency nephrectomy was also performed and demonstrated face and content validity, amongst 75 residents and 27 experts. Similarly, Cabello et al. [70] demonstrated the use of Thiel-embalmed cadavers in renal transplantation and demonstrated face validity amongst 28 subjects. However, face and content validity is generally considered low level of evidence, and further higher-quality studies are needed to prove the use of cadavers for such training. Nevertheless, expert and participant opinion in the included studies highly recommends cadaveric training and suggests they be utilised as masterclasses.

12.3.8 Non-technical Skills Simulation

Considerable attention has been given to the development of technical skills in the simulation environment. Three distinct categories of non-technical skills are often described in the literature

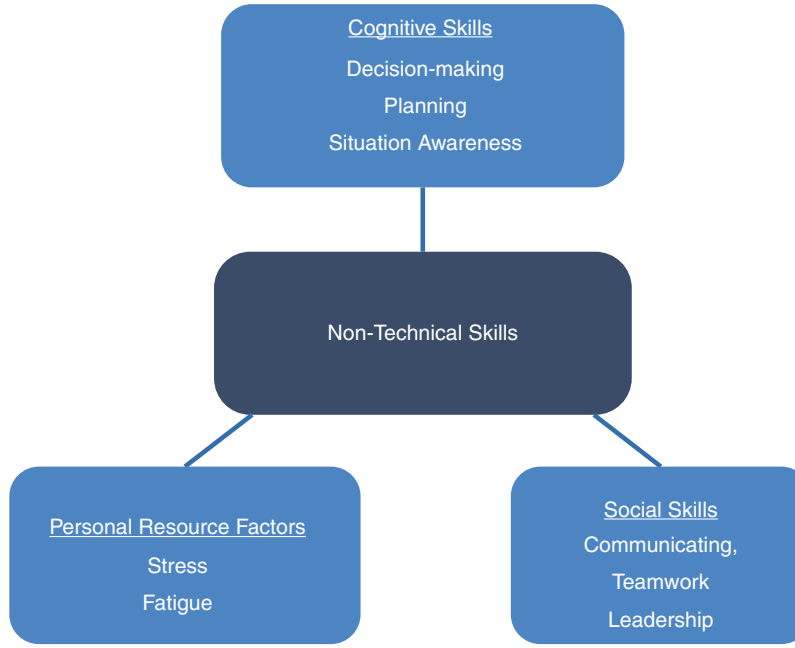

Fig. 12.2 Components of non-technical skills

including cognitive skills, personal resource factors and social skills [71] (Fig. 12.2). A number of different concepts have been utilised for integration of non-technical skills and team training in urology [72–76].

A high-fidelity OR was utilised within two studies [75, 76] using the SIMPLE model. The authors executed a partial nephrectomy scenario with complications. High-fidelity OR team training demonstrated face, content and construct validation in both technical skills and non-technical skills. TeamSim (Surgical Science) is another example of team training package where a virtual OR can be created alongside the LapSim for procedural training. However, it remains to be validated.

Team training is also a very important concept in robot-assisted surgery due to the setup of the operating room. The surgeon is at the console, away from the patient, and, thus, relies on assistants for the safety of the patient. The Xperience® Team Trainer (XTT, Mimic Technologies) is developed to train both the surgeon and the assistant. Although it is currently used alongside generic skills modules, it is hoped that procedure-specific modules will also be developed. The platform has demonstrated face, content, construct and concurrent validity [77].

A cheaper alternative is full immersion distributed simulation (Imperial College, London, UK), a low-fidelity portable and inflatable simulated operating environment with integrated audio-visual equipment, operating light and posters depicting the real OR [78]. It has been utilised and validated for technical and non-technical skills training for ureteroscopy [72], transurethral resection [74] and GreenLight laser prostatectomy [79]. The former study also confirmed a strong correlation between technical and non-technical skills [73]. Ross et al. [80] utilised this concept for robotic surgery training and demonstrated construct validity of technical and non-technical skills between 22 novice and 14 intermediate and expert participants.

Conclusions

Advances in minimally invasive surgery, early-stage diagnosis of disease and pharmacological developments have resulted in a reduction in the number of patients requiring major urological surgery. This change in practice in

combination with reduction in working hours makes it imperative to look at alternative means of training to shorten the learning curve and improve patient safety. In the absence of procedure-specific models, basic skills acquisition could aid and reduce the initial phase of the learning curve. This, followed by effective utilisation of modern workplace-based training, can be implemented in order to provide future surgeons with the skills and knowledge required to operate in a safe manner with successful outcomes.

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The Future of Robotic-Assisted Partial Nephrectomy

13

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Abbreviations

eGFR	Estimated glomerular filtration rate
ICG	Indocyanine green
LPN	Laparoscopic partial nephrectomy
NIRF	Near-infrared fluorescence
PN	Partial nephrectomy
RPN	Robotic partial nephrectomy
WIT	Warm ischaemia time

Key Messages

1. The innovation in field of partial nephrectomy has been rapid over the last century, and the current technologies could not have been predicted.
2. Looking to the future, new robots and new adjuncts to the robots will become more accessible and more widespread.
3. Increasing use of image-guided surgery and intraoperative fluorescent imaging has supported greater vascular dissection as well as excision of the tumour itself.
4. A number of new robotic surgical systems are eagerly anticipated, providing further technological advances such as haptic feedback.
5. A key challenge is the development of a cost-effective platform to enable widespread delivery of robot-assisted surgery.

13.1 Introduction

Urologists have a strong history of embracing innovation, and partial nephrectomy serves as an excellent example of how technology may be effectively harnessed. A wide range of new techniques and technologies are being developed, yet the central objectives remain the same. These are

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to (1) preserve renal parenchyma, (2) optimise preoperative estimated glomerular filtration rate (eGFR) and (3) reduce global warm ischaemia time (WIT). All three have shown to be important predictors of post-operative renal function, and it is hoped that improvements in these areas will lead to further gains in patient outcomes.

13.2 Clamping: Variations on a Theme

Renal vascular clamping helps limit blood loss and provides a clear operative field for tumour excision and renal reconstruction/renorraphy. However, excessive clamping time risks permanent loss of renal function. Various recent techniques have been proposed to reduce WIT and improve renal outcomes.

13.2.1 Off-Clamp Partial Nephrectomy

Partial nephrectomy (PN) without any clamping of the renal pedicle has been performed. Renal ischaemia is completely abolished at the expense of increased blood loss and more difficult renorrhaphy with the potential for occasional disaster. Techniques to control 'off-clamp' bleeding have been explored with mixed success, for example, application of manual compression of the peri-tumoural parenchyma or using Kauffman clamps [1].

Results using 'off' and 'on' clamp techniques have been compared in a recent meta-analysis [2]. No significant differences were found in operative times, complications rates or length of stay. A trend was seen towards increased positive margins, blood loss and transfusion rates in the off-clamp group, which could be explained by impaired visualisation, but this difference did not reach statistical significance (Fig. 13.1).

A significantly lower reduction in eGFR was associated with off-clamp PN (Fig. 13.2) [2]. Critically it is not clear whether this corresponds to a reduced risk of CKD. Some studies showed a loss of any difference between 'off' and 'on' clamp techniques by 3 months if WIT is kept to below 30 min [2]. Conversely others studies have shown a reduced risk of new onset CKD with 'off clamp' when followed up [3].

In summary it appears that current evidence suggests that the off-clamp technique for PN when compared to on-clamp PN leads to a reduced risk of acute kidney injury after surgery, but the benefit to long-term renal function is less clear. Off-clamp techniques may be associated with slightly higher intraoperative blood loss and transfusion rates (although no statistically significant difference), but with similar positive margins and complication rates highlighting potential for this technique. There remains, however, the

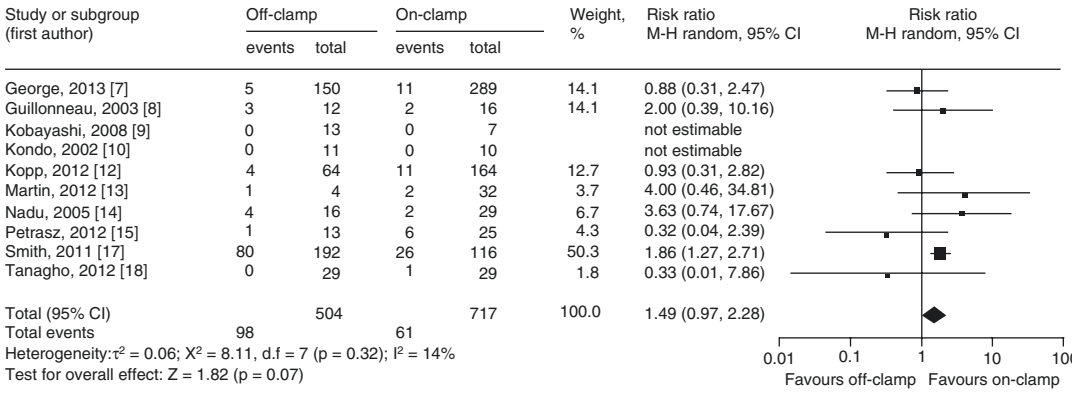

Fig. 13.1 Meta-analysis of blood transfusion rates [2]

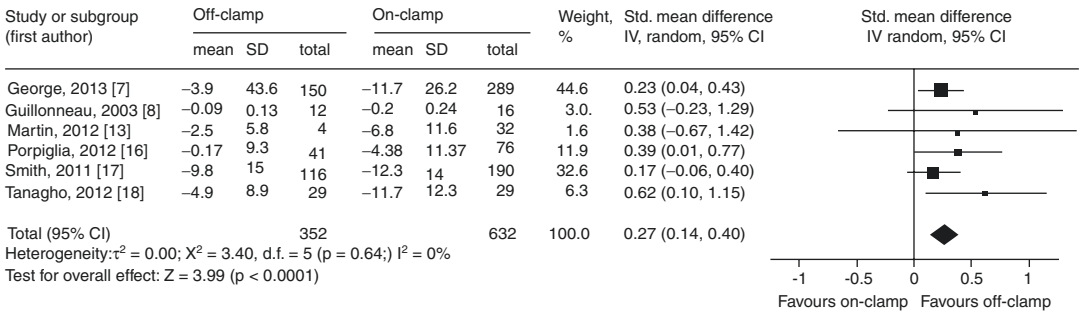

Fig. 13.2 Meta-analysis of change in eGFR [2]

potential danger for significant and uncontrollable bleeding leading to nephrectomy.

13.2.2 Early Unclamping

Early unclamping involves the removal of clamps immediately after placement of the initial deep running suture and prior to the placement of subsequent outer or bolster sutures into the renal cortex. In LPN the technique reduces WIT by >50% with improved post-operative renal function up to 90 days post-operatively [4]. In comparison, given the shorter overall WIT seen with RPN, the physiological benefits of shortening the WIT by 3–5 min will be difficult to establish. The method does risk higher blood loss, but studies have shown no effect on transfusion rates or haemorrhagic complications even with complex renal tumours or less experienced surgeons [5]. It has also been hypothesised that early unclamping may lead to reduced rates of post-operative haemorrhage, as arterial bleeds will be easier to identify in perfused kidney [4].

13.3 Fluorescence Image-Guided Robotic Surgery and Selective Arterial Clamping

Use of fluorescence image guidance during RPN offers two principle benefits. Firstly, better identification of the tumour will permit a more accurate dissection and greater preservation of renal parenchyma. Secondly, better delineation of the renal vascular anatomy will enable selective arterial clamping, reducing unnecessary ischaemia within healthy and non-tumour-bearing renal parenchyma.

The technology uses near-infrared fluorescence (NIRF). A fluorescent contrast agent is administered intravenously, which emits light in the near-infrared wavelength (700–850 nm) after activation by a light-emitting diode. The light, invisible to the human eye, is recorded using a charge-coupled device camera. The most widely used tracer is indocyanine green (ICG), but others approved for clinical use include protoporphyrin IX, d-aminolevulinic acid (ALA), hexylaminolevulinate (HAL) and fluorescein. Indocyanine green (ICG) is injected intravenously and can be identified throughout the vascular system in less than 1 min. It has four properties that make it ideal for this purpose; it remains within the vascular compartment after administration, has a short plasma half-life of 3–5 min, is cleared by hepatic metabolism (and is not nephrotoxic) and can be detected by the NIRF camera [6]. It can also be used for the identification of tumour margins since the fluorescence varies between normal tissue, tumour, cysts and necrotic fat. Three systems are currently available for use in laparoscopic/robotic surgery: the SPY Imaging System (Novadaq Inc., Missisaugua, ON, Canada), the Storz D-Light (Storz GmBH, Tuttlingen, Germany) and the Firefly system which incorporates the SPY system directly into the Da Vinci Si and XI. This allows the surgeon to

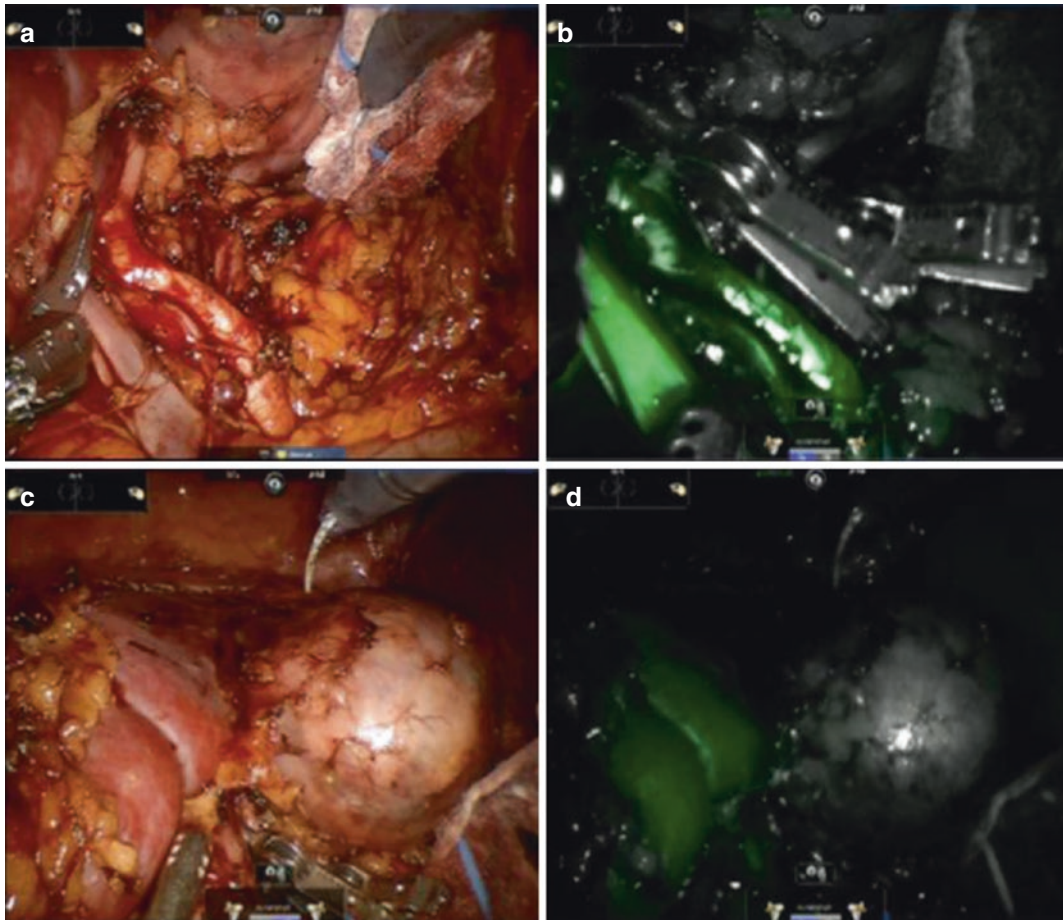

Fig. 13.3 NIRF imaging with ICG to facilitate selective arterial clamping. (**a**, **b**) Dissection of the secondary, tertiary or quaternary level arterial branches using mini bulldog clamps. (**c**, **d**) Renal tumour seen under white light and NIRF, with the hypo-fluorescent renal tumour confirming ischaemia with perfused *bright green* normal renal parenchyma [13, 18]

switch between standard (white) light and fluorescence-enhanced views in real time (Figs. 13.3 and 13.4).

13.3.1 Selective Arterial Clamping Using NIRF

Selective arterial clamping minimises unnecessary ischaemia and reperfusion injury thereby preserving renal function [7]. NIRF is used to accurately identify the renal vasculature, assess renal perfusion and dictate the arteries that need to be clamped. The technique allows the surgeon to clamp only those segmental arteries that supply the tumour and its immediate margin whilst maintaining perfusion of rest of the renal parenchyma [8]. Before administering the ICG, the major arterial branches should be clamped with micro bulldog clips. Once the dye has been given, each clamp is released individually to identify the areas of perfusion. This technique shows great promise. Compared to standard arterial clamping, early results showed significant improvements in post-operative kidney function at discharge, and a trend towards significance at 3 months [8]. Other methods of selective arterial clamping have been trailed, for example, colour Doppler ultrasonography. However, given the complexity of the technique and the technology

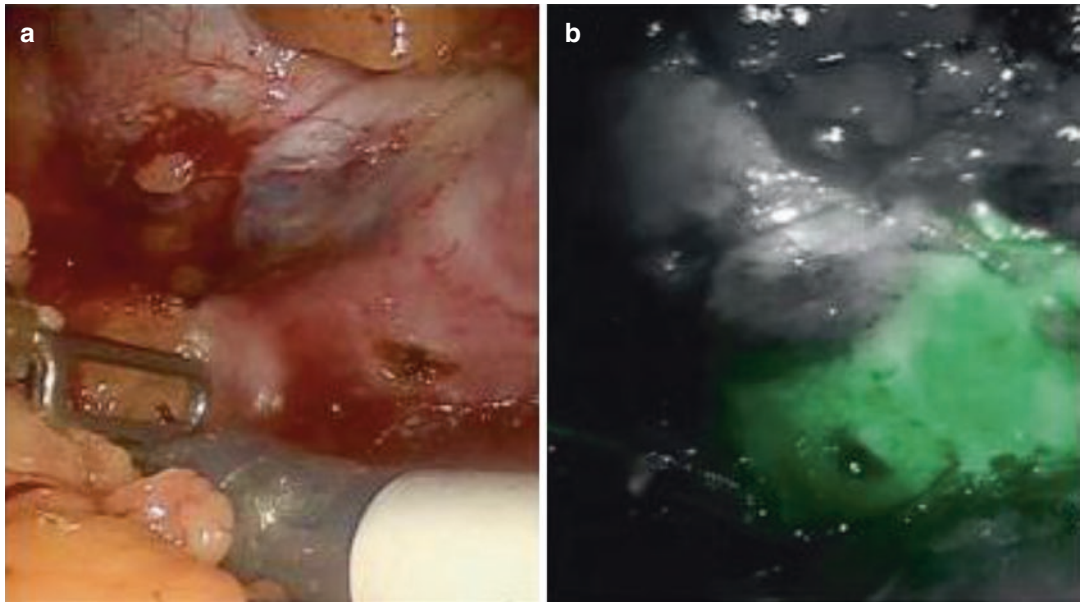

Fig. 13.4 (**a**) White-light image of a renal tumour. (**b**) Corresponding NIRF image of the same renal tumour. The tumour shows no fluorescent properties. Photo credits: Advances in Image-Guided Urologic Surgery. Edited by Joseph C. Liao, Li-Ming Su. Springer, 18 Nov 2014

being very operator dependent, uptake has been very limited.

The main limitations to NIRF are the high costs of the Firefly system together with limited evidence of longer-term benefits. Given the good long-term renal function and very low dialysis rates already achieved following RAPN, Firefly will need to demonstrate a significant clinical benefit to justify the additional cost.

In conclusion, available evidence suggests that RPN with NIRF provides an improvement of the preservation of renal function at discharge; however, this effect may diminish with time. Its use may therefore be restricted to complex cases or patients with impaired renal function to minimise warm ischaemia.

13.3.2 Using NIRF to Identify Renal Tumour Margins

NIRF has the capability to help differentiating between tumour and normal tissue. This improved accuracy may not only enable improved dissection and consequently better preservation of healthy parenchyma but may also enable faster dissection helping to reduce WIT.

Given that the positive margin rate in RPN is already extremely low (around 3–5% in most series), it is difficult for a study investigating NIRF to have adequate power to show a difference in positive margin rate. Thus, current studies do not show that NIRF decreases positive margin rate or even Clavien III–IV complications [9].

13.4 Image-Guided Surgery

Image-guided surgery aims to improve intraoperative visualisation through the use of preoperative and/or intraoperative images used either alongside or integrated with the real-time endoscopic images. For partial nephrectomy in particular, ICG has been used to aid the early recognition of vessels and the vascular dissection of the kidney as well as excision of the tumour itself.

Image-guided surgery may use either preoperative or intraoperative images. Various active intraoperative imaging modalities are used including CT and MRI. Yet whilst active intraoperative CT and MRI imaging is used in orthopaedics and neurosurgery, its use in urology is likely to be limited. Currently the cost of intraoperative scanners remains prohibitively high, and although portable scanners are becoming cheaper, the lack of soft tissue discrimination for the kidney and suboptimal spatial accuracy restricts their use. Currently the most widely used form of intraoperative imaging in urology is ultrasound. Drop-in AU2324 US probes (e.g. ProART Robotic Drop-In 8826 probe, BK Medical, MA, USA) are routinely used for identifying the renal vasculature and to delineate tumour margins.

The second type of image-guided surgery incorporates preoperative images into the visual display of the surgeon. Preoperative 3D images are transformed and mapped to the 3D patient anatomy, a process known as registration. A mesh overlay system then allows the surgeon to see the underlying anatomy without visual impedance (Fig. 13.5). A recent study by the University of Florida College of Medicine and Johns Hopkins University demonstrated a technique to increase surgical confidence in excision.

TilePro™ software allows multi-input displays from two data sources to be shown simultaneously beneath the surgical field at the console. This software uses a CT scan to create a 3D reconstruction of the organ. These images can then be available to the surgeon alongside the 3D endoscopic operative video feed (Fig. 13.6).

However, the system is limited by intraoperative variations in the kidney's anatomy [10]. Automated segmentation software to obtain precise segmentation is under development. There have also been concerns raised regarding the

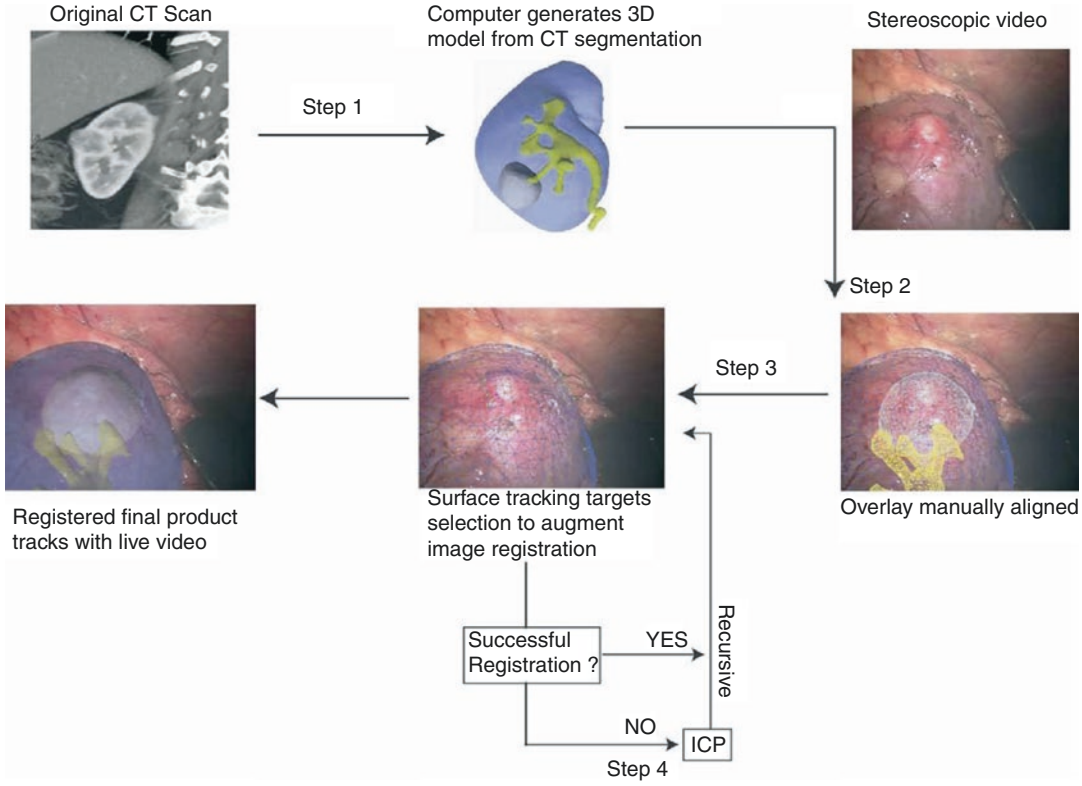

Fig. 13.5 Flowchart of steps for 'registration' of preoperative CT images to live stereoscopic video (ICP iterative closest point registration) [19]

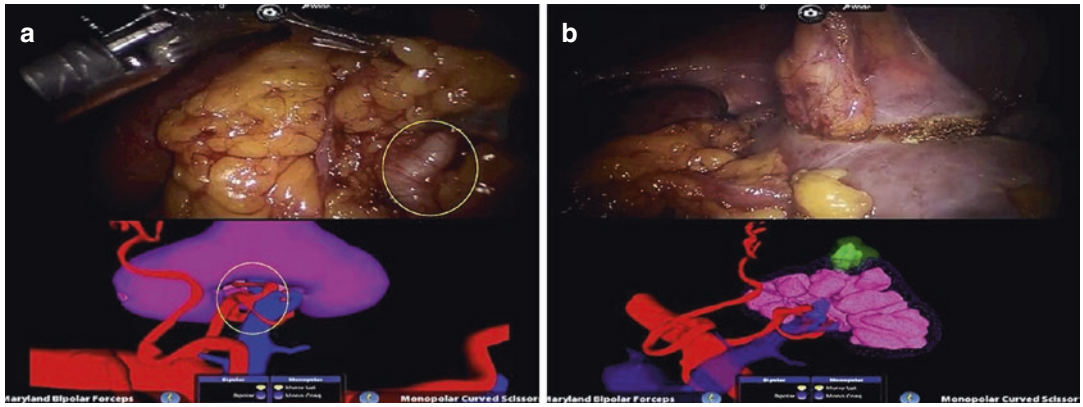

Fig. 13.6 The console view with TilePro enabled. (**a**) The hilar anatomy with more clarity to better appreciate the anatomy in the operative view. (**b**) The surface of the kidney as a polygon mesh whilst keeping the tumour solid to aid dissection [20]

safety of image overlay, with surgeons more likely to exhibit inattention blindness, but the risks have not yet been formally assessed [11].

13.5 Renal Hypothermia/Cooling

Tissue hypothermia has been found to be effective in reducing ischaemic damage in various organs. Renal hypothermia allows clamps times of up to 3 h by slow renal metabolism providing cellular protection and limiting reperfusion injury [12]. Reducing renal ischaemia injury also prevents the release of inflammatory and vasoactive peptides that cause further tissue damage. Various techniques for cooling the kidneys have been proposed. Perirenal ice slush, cold saline surface irrigation, endoscopic retrograde renal cooling and trans-arterial renal hypothermia have all been described with varying degrees of success. An elegant technique, described by Gill et al., placed the kidney within an endocatch filled with ice slush to achieve a temperature of 5–19° [13]. An alternate method that avoids having to use a cumbersome bag makes use of a GelPoint port (Applied Medical, CA, USA) to pack ice on the psoas muscle and around the renal parenchyma [14]. The disadvantage of this technique does risk obscuring the operative field with ice slush.

13.6 Laser Technology

The use of various lasers has been trialled for dissection due to their haemostatic properties. Early studies used neodymium-doped yttrium aluminium garnet (Nd:YAG), potassium titanyl phosphate (KTP) and holmium yttrium aluminium garnet (Ho:YAG) lasers; however, they were limited to isolated case series. Both suffered problems from excessively deep cutting and smoke formation. More promising work has been undertaken using diode and thulium lasers. Thulium lasers have excellent cutting and coagulation properties and emit a continuous rather than pulsed wave. Liberal irrigation can be used to limit problematic smoke formation and tissue carbonisation [15]. Primary concerns regarding their use centres on the potential difficulty in identifying tumour margins due to charring artefact and unrecognised collecting system injury.

13.7 Developments in Robotic Technology

The latest edition of surgical robot, Da Vinci Xi by Intuitive Surgical®, offers several new features advantageous in partial nephrectomy such as integration of the Firefly system and improved

access. Similarly developments to accompanying equipment help have been found to be helpful. A recent innovation is the Table Motion device (TruSystem® 7000dV table) which permits considerable table adjustments during a robotic surgical procedure, not previously possible. Virtual fixtures or barriers have been created by Microsoft's Kinect video technology (Microsoft Inc., Redmond, Wash), whereby haptic telemanipulators cause the surgeon to 'feel' the robotic instrument hitting a virtual barrier set by the surgeon [16]. This would help preserve oncological margins or vital structures.

The development of new surgical robots is highly anticipated. Several systems are currently being developed offering a number of new technologies over the Da Vinci system. The only system with regulartory approval is the Alf-X by TransEnterix (TransEnterix Inc., NC, USA) which gained the European CE mark in 2011. A number of clinical trials in humans have already been published. Early results have shown that the robot offers outcomes comparable to that of laparoscopy, but further studies are awaited for a comprehensive assessment of the system [17]. Others under development include Titan Medical Inc.'s SPORT Surgical System in addition to systems by Medtronic (Medtronic, MS, USA) and a Verb Surgical (Verb Surgical Inc., CA, USA), collaboration between Google and Johnson & Johnson. A key feature of these new robotic systems is the incorportation of haptic feedback, a major limitation of the Da Vinci system. Another major potential advantage of these new contenders is greater price competition.

Conclusions

The future of robotics lies in integrated imaging and navigation, with augmented reality and inclusion of haptic and sensory capabilities providing more targeted treatment of tumour resection. The real challenge is in providing a cost-effective robotic platform to provide for the majority of patients.

Whereas the capability and results of the surgeon were previously based on cognition, vision, technique and dexterity, the urologist of the future may be the manager of connectivity, creativity and supervisor of surgery by automated intelligence.

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Challenging Situations in Robotic Partial Nephrectomy

14

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Abbreviations

ESRD	End-stage renal disease
MIS	Minimally invasive surgery
NSS	Nephron-sparing surgery
OR	Operating room
PN	Partial nephrectomy
PSM	Positive surgical margin
RCC	Renal cell carcinoma
TA	Thermal ablation
VHL	Von Hippel-Lindau

Key Messages

- Growing experience of partial nephrectomy has enabled surgery to be offered to patients previously considered too complex.
- Prior abdominal surgery can greatly increase the complexity of a partial nephrectomy and requires careful preoperative and intraoperative planning.
- Horseshoe kidneys may be complicated by aberrant vascular anatomy particularly if a heminephrectomy is required.
- The two primary aims in managing single functioning kidney are to gain oncological control and maintain sufficient renal function.
- The safe management of complex patients requires a well-planned, multidisciplinary approach by teams experienced in treating such patients.

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14.1 Introduction

Increasing detection of asymptomatic small renal masses has resulted in a significant stage migration of renal cell carcinoma (RCC). Together with a growing recognition of the importance of the preservation of renal function alongside cancer control, this has led to a

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significant shift in treatment towards nephron-sparing techniques. For T1 tumours in healthy patients, partial nephrectomy is now considered the standard extirpative technique. Superior functional and equivalent oncological outcomes have led to it being favoured over radical surgery for both T1a and T1b tumours when feasible. However, the indications for partial nephrectomy continue to expand particularly in atypical cases such as patients with single functioning kidneys, poor kidney function, anatomical anomalies and hereditary syndromes predisposing to multiple kidney cancers, such as Von Hippel-Lindau syndrome. With the growing body of experience, the indications continue to expand even in those patients previously considered too complex. Nonetheless, such scenarios still pose significant surgical challenges. The key challenging situations a renal surgeon may face are outlined in this article together with advice on how these particular circumstances should be handled.

14.2 Prior Abdominal Surgery

Prior abdominal surgery may greatly increase the complexity of a partial nephrectomy especially for the robotic surgeon. Prior surgery is associated with a much higher risk of intra-abdominal adhesions making access difficult or even impossible [1]. Patients need to be consented appropriately and understand the increased risks of conversion to open surgery and injury to vascular or visceral structures in particular to the bowel. Prior abdominal surgery has also been shown to lead to increased operative times and higher complication rates during laparoscopic surgery [2, 3].

Thorough preoperative planning involving the whole surgical team is vital. Understanding exactly what previous surgery was performed, the technique and indication is paramount. Reviewing the previous operation report or even having a discussion with the surgeon can be extremely beneficial. For example, large bowel operations, ruptured appendix and inflammatory bowel diseases are more likely to cause greater adhesions [1].

In difficult cases, it is sensible to choose the most experienced operating room (OR) scrub staff and surgical assistants. A reliable, familiar team who understand the intricacies of robotic surgery and can troubleshoot unexpected problems is very important in these situations.

The next step is to decide on which approach to take. A retroperitoneal approach may be more suited if the patient has had prior abdominal surgery, particularly with posterior renal lesions. Its disadvantages are the lack of space and that it is often a less familiar approach for the surgeon. Whichever approach is chosen, a final decision on the feasibility and precise approach to the kidney can often only be made once the camera port has been inserted. Based on the degree of adhesions, the surgeon must determine where the remaining ports can be inserted safely. Several techniques can be used to gain access. No device or technique is perfectly safe, and there is no consensus regarding the optimal choice, although, in the opinion of the authors, if in doubt the open Hassan technique is likely to be safer than a blind Veress needle insertion. If using a Veress needle technique, it should be inserted at a distant site to previous incisions. Optical trocars are not recommended in these situations.

The remaining instrument port positions can then be triangulated. Knowledge of optimal distances is important to prevent the robotic arms from clashing. Ports need to be at least 8 cm apart and 10–20 cm from the target anatomy when using the Da Vinci Si. The newer Da Vinci Xi permits closer port placement with a minimum distance of 6 cm. Tapping the skin at the intended insertion site helps the surgeon to visually determine if it is safe to place a trocar. If unsure, a spinal needle can be inserted through the skin, and its trajectory can be followed with the camera to ensure there is no interposed bowel. An advantage of the Xi is that the camera can be inserted through any of the robotic ports, allowing the surgeon to visualise the insertion of other ports from different angles. This is particularly useful when placing the assistant ports.

Adhesiolysis with laparoscopic scissors may be necessary to permit the safe placement of additional robotic ports after placement of an initial

trocar. Alternatively, a single robotic arm can be docked first in order to take down the adhesions with the robot scissors. The remaining ports can then be inserted, and arms docked safely. A recent study on transperitoneal robotic partial nephrectomy showed that patients with prior abdominal surgery were more likely to require adhesiolysis (41% vs. 15%, $p = 0.005$). Adhesiolysis took a mean time of 32 min, yet overall no statistically significant difference in operative time was found. In the prior abdominal surgery group, a trend towards longer median warm ischaemia time (21 min vs. 16 min) and median estimated blood loss (150 mL vs. 100 mL) was seen, but this did not reach statistical significance. There were no significant differences in intra- or post-operative complications [1]. Whilst transperitoneal robotic partial nephrectomy may therefore be considered feasible in the setting of prior abdominal surgery, the surgeon must remain vigilant of the many potential pitfalls.

14.3 The Horseshoe Kidney

There are few reported cases of robotic surgery performed for small renal masses in horseshoe kidneys. With an incidence rate of 1 in 400 and a 2:1 ratio in men, horseshoe kidneys are the most common renal fusion anomaly. They appear more often with chromosomal aneuploidies (trisomy and Turner syndrome) [4]. Fusion of the inferior portion of the metanephric blastema during the sixth week of gestation forms the isthmus. As a result, renal ascent is limited by the inferior mesenteric artery at the level of L3. Furthermore, the orientation of the kidney is altered. The hilum is rotated into a medial rather than anterior position and the renal axis tilted with the upper pole lying posteromedially to the lower pole [5]. The vascular supply of a horseshoe kidney is typically highly variable. Renal vessel may arise from any of the neighbouring vessels including the aorta, inferior mesenteric artery, iliac vessels or even sacral artery. Multiple renal arteries are found in 70% of horseshoe kidneys. In addition an artery to the isthmus is also common with 65% originating from the aorta and 35% from the IMA, main renal artery or iliac vessels [6]. The isthmus commonly lies anterior to the aorta and vena cava but rarely may pass between the inferior vena cava and the aorta or even behind both great vessels. As a consequence of their malrotation, the ureters from a horseshoe kidney have to either travel in front of the isthmus or over the anterior surface of the kidneys. This course, lateral to the lower pole calyces, results in the classic intravenous pyelogram findings.

Although most horseshoe kidneys are asymptomatic, complications can include pelviureteric junction obstruction (up to 30%), renal calculi, urinary tract infections, vesicoureteric reflux (up to 50%) and a twofold risk of Wilms' tumour [7]. Rates of other renal tumours are comparable to the general population. Renal cell cancer accounts for 45% of all tumours in horseshoe kidneys. Wilms' tumour accounts for 28% of malignant lesions. Transitional cell cancer and sarcoma account for 20% and 7% of tumours, respectively [8].

This highly variable and aberrant anatomy makes robotic oncologic surgery in patients with horseshoe kidneys very technically challenging. Adequate preoperative imaging is crucial. A triple-phase CT or MRI with three-dimensional arterial reconstruction is strongly encouraged. A skilled bedside assistant with suitable laparoscopic experience is important to ensure safe application of clips and staples using a standard laparoscopic technique [9].

A robotic partial nephrectomy or hemine-phrectomy in a horseshoe kidney can be performed using either a transperitoneal or a retroperitoneal approach. The latter may be essential for posterior tumour as a horseshoe kidney does not allow traditional mobilisation and flipping of the kidney [10].

For a transperitoneal approach, the positioning of the patient is similar to that used in a standard robotic partial nephrectomy, with the patient in a flank position. Standard port positions need to be adjusted, with arms placed more medially and cranially. A fourth robotic arm is recommended for retraction.

The first step is to reflect the colon to expose the aorta and IVC. The ureter and the renal

pedicle should then be carefully dissected out. During this phase, it is important to be vigilant for anomalous arterial branches and dissect them out in preparation for hilar clamping. It should be remembered that with a horseshoe kidney, the majority of the vessels are found above the isthmus [8]. Following excision, reconstruction may be performed using a running 3-0 Monocryl and interrupted 0 Vicryl sutures for the parenchyma and capsule, respectively. It should be noted that even after unilateral clamping, the kidney will still be supplied by the other moiety. Whilst this can make dissection very challenging, it does reduce the risk of ischaemic renal injury.

If a heminephrectomy is necessary, full mobilisation of the kidney is required in order to allow for safe division of the isthmus. Various laparoscopic techniques have been described. For example, a Satinsky clamp may be placed around the isthmus prior to sharply dividing it and then running a 2-0 Vicryl for parenchyma haemostasis [11]. Alternatively a 15 mm Hem-o-lok clip may be applied to the isthmus before dividing it and using a PDS endoloop for haemostasis [8]. Direct transection of the renal isthmus using a laparoscopic stapler has also been described [9].

In all cases, the challenging anatomic variations of horseshoe kidneys should be approached with caution. It is strongly recommended that such cases not be undertaken by novice or intermediate robotic surgeons. The few reported cases in the literature do support the feasibility and safety of robotic partial nephrectomy and heminephrectomy in a horseshoe kidney albeit in expert hands. However, meticulous attention to the patient's vascular anatomy is paramount to avoid bleeding complications. Port placement needs to be individualised to avoid instrument clashing and to facilitate optimal access to the kidney [12].

14.4 Single Functioning Kidney

One of the most common challenging situations a renal surgeon will encounter is that of the patient with a single functioning kidney. Close attention needs to be taken to manage the discordant risks of renal cancer and chronic renal failure with the associated cardiovascular risk and increased mortality [13]. In view of this, the two primary aims in the management of such patients are to attain adequate oncological control whilst maintaining sufficient renal function. Chronic kidney disease is encountered in a large proportion of patients with small renal masses [14], but the significantly lower preoperative estimated glomerular filtration rate (eGFR) of patients with solitary kidneys highlights their vulnerability [15]. A single functioning kidney is one of the most significant risk factors for developing renal failure following nephron-sparing surgery (NSS) [7].

Partial nephrectomy, despite the risks, remains a feasible management option that may help the patient avoid dialysis. Yet the factors determining post-operative eGFR remain under debate [16]. La Rochelle et al. found that the only relevant variables were cold ischaemia time and the presence of cardiovascular risk factors [17]. In addition, these factors were only found to affect the immediate post-operative renal function; none were associated with long-term eGFR. Tumour size was also shown not to cause an effect on long-term eGFR by another single centre study; however, the authors did show that clamp time and blood loss were significant predictors of post-operative eGFR but only in the short term [15]. Concerns regarding prolonged are especially pertinent in the setting of significant preoperative renal impairment [18, 19]. However, large studies have found that in the long term, ultimate renal function is primarily determined by the amount of parenchymal loss rather than the degree of ischaemia injury [20]. After an initial post-operative fall in eGFR, studies have shown that long-term renal function remains relatively stable following partial nephrectomy, and the need long-term dialysis remains uncommon [17, 20]. The risk of dialysis has been found to correlate to preoperative eGFR; patients with the poorest preoperative renal function are at the greatest risk of end-stage renal disease (ESRD) [17].

Oncological safety is of paramount importance for NSS in solitary kidneys. Given the bleak outcomes for patients on dialysis, avoiding radical surgery is vital. The most significant risk

Table 14.1 Outcomes for partial nephrectomy in single kidneys

Study	Date	Approach	Outcomes
Ghoneim et al. [10]	2015	Open partial nephrectomy, *n* = 103	5-year OS = 64% 5-year CSS = 81%
Ching [13]	2013	Open partial nephrectomy, *n* = 282	5-year OS = 78.5% 5-year CSS = 95.1% 5-year RFS = 75.4% 10-year OS = 59.5% 10-year CSS = 91.9% 10-year RFS = 70.8%
Lee et al. [19]	2011	Open partial nephrectomy, *n* = 38	5-year OS = 59.6% 5-year CSS = 77.5% 5-year RFS = 45.7%
La Rochelle [12]	2009	Open partial nephrectomy, *n* = 68	5-year CSS = 89% (no prior metastatic disease)
Pahernik [60]	2007	Open partial nephrectomy, *n* = 103	5-year OS = 80.1% 5-year CSS = 89.6% 10-year OS = 54.1% 10-year CSS = 76%
Fergany [61]	2006	Open partial nephrectomy, *n* = 400	5-year OS = 87% 5-year CSS = 89% 10-year OS = 77% 10-year CSS = 82%
Saranchuk [14]	2004	Open partial nephrectomy, *n* = 54	5-year OS = 68% 5-year CSS = 88% 5-year RFS = 73%
Ghavamian et al. [24]	2002	Open enucleation, *n* = 23 Open partial nephrectomy, *n* = 24 Both = 7 Ex vivo tumour resection = 8	5-year OS = 74.7% 5-year CSS = 80.7% 10-year OS = 45.8 10-year CSS = 63.7%

factors to develop ESRD are inadequate resection and local recurrence [20]. Positive surgical margin (PSM) rates have been found to be higher in solitary kidney patients compared to patients with normal contralateral kidneys, but the significance of these findings is debatable. There is evidence to suggest that PSM have negligible effects on development of metastasis whilst other authors argue that PSM do increase the risk of metastasis [21, 22]. Hence, whilst it is argued that tumour enucleation can offer equivalent outcomes to partial nephrectomy, the balance appears to be moving in favour of performing an adequate resection to minimise the risk of PSM.

NSS in solitary kidneys has been shown to be effective with 5-year cancer-specific survival rates of 77.5–88%, similar to those in patients with a normal contralateral kidney (see Table 14.1). Lower overall survival rates in these patients can be attributed to the increased morbidity associated with CKD [16, 23]. When compared to the much poorer survival rates of patients on dialysis, it can be argued that NSS should be considered in all appropriate patients in the setting of a single functioning kidney [24].

Historically open partial nephrectomy was associated with better post-operative renal function than a laparoscopic approach [25]. LPN has been shown to be safe and effective, but success remains highly dependent both on appropriate patient selection and the surgeon's laparoscopic expertise [26]. Alongside techniques adopted from open surgery such as ice slush cooling, other procedures have been incorporated to minimise ischaemia. Those more routinely employed include early unclamping or segmental clamping. Alongside these specific enhancements to the standard PN technique, the benefits of the robotic

platform have also helped overcome a number of the difficulties faced in partial nephrectomy [27]. Precise tumour resection and a faster renorrhaphy help reduce renal injury.

As with 'routine' small renal masses, other treatment modalities have been used in patients with single functioning kidneys. Thermal ablation (TA) offers an alternative, less invasive treatment option. However, given the scarcity of cases, data on experience and outcomes for TA in solitary kidneys remains limited. Analysis of the observational studies that constitute the publish experience of the use of TA in single kidneys shows that whilst PN offers better cancer control, TA is associated with better preservation of renal function and lower complications, thereby offering a viable option for those patients unable to undergo PN [28].

14.5 Von Hippel-Lindau Syndrome

Von Hippel-Lindau (VHL) is the most common hereditary RCC syndrome. Inherited in an autosomal dominant fashion, inactivation of the VHL gene leads to over expression and accumulation of hypoxia-inducible factor 1 (HIF-1) and tumour formation. A variety of tumours may develop including retinal and central nervous haemangioblastomas, phaechromocytomas and pancreatic endocrine tumours. One of the most common and a leading cause of mortality in these patients is RCC. The surgical management of such hereditary, multifocal tumours centres on preventing progression to metastatic disease whilst maintaining native renal function for as long as possible. An essential component of the management of such patient is effective screening. In VHL this commonly consists of performing annual ultrasounds during childhood before progressing to yearly contrast-enhanced CT scans from 18 years. Historically patients with multifocal and recurrent hereditary tumours were managed with bilateral nephrectomy and dialysis with a view to transplantation. Developments in nephron-sparing surgery together with limited availability of donor organs and recognition of the morbidity of even short periods of dialysis have led to the development of new surgical approaches.

Accurate diagnosis is vital for managing VHL patients. When possible renal biopsy should be performed to provide a histological diagnosis as well as for genetic testing [29]. Split renal function needs to be assessed to establish baseline renal function and guide subsequent treatment. Surgical intervention requires careful consideration to minimise renal tissue loss. Bilateral partial nephrectomies may be indicated and can be performed either as a staged procedure or simultaneously, the latter becoming increasingly common. If a staged strategy is used, the largest tumour is usually resected first given the greater risk of metastasis [30]. Alternatively, some surgeons elect to operate on less complicated tumour first. Laparoscopic and robotic techniques have been shown to be feasible in treating multiple renal tumours; however, their use must not come at the expense of oncological clearance [31].

The 3 cm rule is often applied to hereditary renal cell carcinomas during surgical planning. Developed for VHL patients, it dictates that only solid tumours over 3 cm should be treated. The competing risks of oncological safety, nephron preservation and minimising surgical intervention need to be carefully balanced [30]. With the low oncological risk of a small PSM in small renal masses together with the need to minimise renal parenchymal loss, enucleation is considered a feasible technique for managing such patients [32]. Since patients are highly likely to require further surgery, the degree of renal hilar dissection and vascular clamping needs to be cautiously considered. Many surgeons favour non-ischaemic dissection to reduce ischaemic injury, but such an approach relies on competent assistance to maintain a clear surgical field. Larger bleeding vessels should be individually sutured, whilst smaller vessels and generalised bleeding may be managed with haemostatic agents. Avoiding non-specific cautery especially at the base of the defect helps protect segmental

vascular supply. Minimising dissection of the kidney and perseveration of Gerota's fascia with a clam shell incision will help reduce adhesions and the chance of fistula formation between multiple defects [29].

Ablative techniques are increasingly being used for treating VHL, particularly smaller, recurrent tumours. Ablation allows repeated interventions with greater preservation of renal function compared to NSS. Both cryotherapy and radiofrequency ablation have been used effectively in treating VHL patients either on their own or combined with PN.

The success of a careful, targeted management programme for hereditary RCC syndromes such as VHL has been demonstrated by various studies. Herring et al. reported their 10-year experience of managing 50 patients with various hereditary renal cancers. Through a combination of regular screening, avoiding intervention for lesions less than 3 cm and carefully planning surgery, all patients avoided dialysis and only one developed metastatic disease. Similarly good results with no metastatic progression have also been reported by other authors [33, 34].

14.6 Ectopic Pelvic Kidneys

Ectopic pelvic kidneys are uncommon, presenting in 1/10,000 patients, whilst autopsy studies estimate their true prevalence as up to 1/1000. As a result of their short, torturous ureters, pelvic kidneys are more susceptible to infection, calculi and obstruction. The risk of malignancy in ectopically placed kidneys is equivalent to that in the general population, and given their rarity, there are only very limited reports of their management in the literature. Treatment should adhere to the general principles of oncological management, although a number of aspects need careful consideration. The altered anatomy of the pelvic kidney poses a number of challenges. Firstly, the kidney is usually buried deep within the pelvis below the aortic bifurcation and hidden by the sacrum. Medial positioning of the hilum and rotation of the kidney further complicate dissection especially within the confines of the pelvis [35]. Ectopic kidneys maybe also associated with other anatomical abnormalities of the vertebral column and gastrointestinal and urogenital tract altering the anatomy. Secondly, the vasculature, dependent on the position of the kidney, is also liable to be highly variable. The arterial supply may originate from the distal aorta, aortic bifurcation, common or external iliacs or even the inferior mesenteric vessels. Preoperative angiography is therefore recommended to help delineate the anomalous vasculature. Nevertheless, intraoperatively careful but extensive dissection is necessary to prevent inadvertent injury to major pelvic vessels and ureters [36].

Laparoscopic surgery on pelvic kidneys is feasible and has been demonstrated in a number of case series evidence [37]. In contrast only a single case of an open partial nephrectomy in a pelvic kidney has been reported [38]. Aside from this, the literature in managing renal masses in pelvic kidneys is restricted to individual case reports of laparoscopic nephrectomies. However, with reports of robotic and even single site approaches for simple nephrectomies, the first report of minimally invasive partial nephrectomy for a pelvic mass is keenly awaited.

Conclusions

With increasing numbers of patients undergoing partial nephrectomy, the occurrence of some of these special situations is increasing. Whilst the principles remain the same as the standard situations, special attention should be paid to preoperative imaging, multidisciplinary discussions of all treatment options and referral to highly experienced teams if possible. Generally careful choice of approach and access is key in cases of prior surgery, warm ischaemia should be minimised in poorly functioning kidneys, and aberrant anatomy appreciated in anomalies of fusion and ascent. As experience increases, these special situations will increasingly become part of the repertoire of the kidney surgeon.

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Complications and Their Management

15

Peter A. Caputo and Jihad Kaouk

Abbreviations

CKD	Chronic kidney disease
LPN	Laparoscopic partial nephrectomy
NSAID	Non-steroidal anti inflammatory drug
OPN	Open partial nephrectomy
PN	Partial nephrectomy
RAPN	Robot assisted partial nephrectomy

Key Messages

- Complications can be minimised through careful selection of treatment modalities specific to the patient and rigorous preoperative evaluation.
- Positioning injuries are common, and correct patient positioning requires close cooperation between surgical, anaesthetic and nursing teams.
- Surgeons must be vigilant for renovascular complications both intraoperatively and postoperatively.
- Management of urine leaks should be based on three principles: adequate drainage, unobstructed distal flow of urine and treatment or prevention of infection.
- Acute renal insufficiency is more common in patients with pre-existing renal impairment but remains an unfortunate complication of nephron-sparing surgery.

15.1 Introduction

Surgical complications can occur regardless of how vigilant a practitioner may be. However, many complications may be minimised or prevented through rigorous preoperative evaluation and careful individualised selection of a

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treatment modality specific to each particular patient and tumour. When considering treatment options for the small renal masses, one must not only consider patient factors but also surgery-related factors. For example, an equally complex 2 cm mass may be treated completely differently in a 55-year-old patient compared to an 85-year-old patient. Each treatment modality comes with its own risks and benefits, and each should be considered carefully based on the patient's age, comorbid medical conditions and past surgical history prior to subjecting the patient to the risks associated with one's chosen treatment.

Generally the rate of complication for patients undergoing nephron-sparing surgery is significantly higher than the rate experienced by patients undergoing radical nephrectomy. When considering nephron-sparing surgery, we accept a higher complication rate in exchange for lower incidence of chronic kidney disease (CKD).

Thermal ablative therapies have been adopted as a nephron-sparing technique to treat the small renal mass largely due to the decreased complication rate compared to more traditional partial nephrectomy (PN). Thermal ablative therapies such as cryoablation and radiofrequency ablation can be applied laparoscopically or percutaneously. Studies report the complication rate of thermal ablative therapy to be between 8.8 and 19.8% [1–6] (Table 15.1). Other thermal ablative techniques such as microwave ablation, high-intensity focused ultrasound and irreversible electroporation are still in their infancy and need further study prior to routine treatment of patients with a small renal mass.

PN via the open approach is the gold standard for the treatment of small renal masses. Laparoscopic partial nephrectomy (LPN) has been adopted slowly due to the difficulty of laparoscopic suturing. The introduction of robotic-assisted laparoscopy eased the technical burden of laparoscopic suturing making robotic-assisted partial nephrectomy (RAPN) a more popular option in the treatment of small renal masses. PN carries a complication rate between 4.1 and 35.7% [7–18] (Table 15.2). PN subjects patients to a higher rate of complication than does thermal ablative techniques. The higher risk of complication after PN compared to thermal ablative therapy is accepted in healthy patients due to the better oncologic outcomes obtained by extirpative surgery.

15.2 Positioning Injuries

Patient positioning prior to surgery is an important process and should be treated as such. The surgical, anaesthetic and nursing teams should work together to ensure appropriate patient positioning has occurred. Positioning injuries are common and likely underreported. Soft tissue, vascular and nervous system injuries are possible if care is not taken to correctly position the patient.

Table 15.1 Reported complication rates of thermal ablative therapies

	Series	Technique	Procedure number	Tumour size (cm)	Major (%)	Minor (%)	Complications (total %)
CA	Duffey et al. [4][a]	Lap, perc, open	116	2.76	1.7	18.1	19.8
	Klatte et al. [5][b]	Laparoscopic	1177	2.4	10.2	6.8	17.0
	Buy et al. [3][c]	Percutaneous	122	2.6	7.4	4.1	11.5
	Breen et al. [2] [c]	Percutaneous	153	3.32	4.6	5.9	10.5
	Atwell et al. [1] [c]	Percutaneous	311	3.2	7.7	4.5	12.2
RFA	Ramirez et al. [6] [a]	Laparoscopic	79	2.2	3.8	5.1	8.8
	Atwell et al. [1] [c]	Percutaneous	254	2.1	4.7	5.1	9.8

[a]Major complication defined as Clavien grade 3 and above
[b]Systemic review; Major and minor complications determined by AUA complication grading scheme
[c]Major complication defined as Clavien grade 2 and above

Table 15.2 Reported complication rates or PN

	Series	Procedure number	Tumour size (cm)	Major (%)	Minor (%)	Complication (total %)
Open	Springer et al. [15]	170	2.9	1.8	4.1	5.9
	Ficarra et al. [8]	200	[a]	4.5	17.0	21.5
	Gill et al. [9]	1028	3.5	–	–	19.2
	Gill et al. [10]	100	3.3	1.0	12.0	13.0
	Mason-Lacomte et al. [12]	58	3.1	3.4	10.3	13.9
Lap	Zargar et al. [18]	646	2	5.8	15.1	20.9
	Porpiglia et al. [14]	206	3.3	5.8	10.7	16.5
	Springer et al. [15]	170	2.8	0	4.1	4.1
	Wheat et al. [17][**]	336	2.8	6.6	29.1	35.7
	Gill et al. [9]	771	2.7	–	–	24.9
Robotic	Zargar et al. [18]	1185	2.3	3.3	11.5	14.8
	Tanagho et al. [16]	886	3.0	3.6	12.1	15.6
	Mathieu et al. [13]	240	3.0	10.4	22.5	32.9
	Kaouk et al. [11]	400	3.17	3.3	12.0	15.3
	Ficarra et al. [7]	347	2.8	2.9	8.9	11.8

Major complications defined as Clavien grade 3 or above, unless otherwise noted
[a]85.5% of patients in study arm had cT1a tumours
[**]Major complication defined as National Cancer Institute Common Toxicity Criteria ver 2.0 grade 3 and above

The lateral decubitus position is most frequently used in operations of the kidney and retroperitoneum for the treatment of the small renal mass. Padding all pressure points paying particular attention to the feet, ankles and knees can prevent soft tissue injury [19]. The most bothersome to patients however is neurapraxia, nervous injury that can occur either by stretch, compression or ischaemia to the nerves of the brachial plexus [20]. The lateral decubitus position can lend itself to brachial plexus nervous injury due to compression injury on the down side or stretch injury on the up side. The weight of the patient lying on the arm will compress the clavicle and first rib against the nerves supplying the arm. The nerves of the contralateral brachial plexus are injured from stretch of the arm being fixed in an over-abducted position or in the case where the head is not supported and allowed to hang onto the table. The use of an axillary roll, a rolled sheet or a silicone bump, will prevent compression injury to the down side and should be placed at approximately the level of the areola in men or slightly inferior to the axilla in women. The contralateral arm should be supported at a 90° angle from the thorax with care taken not to over abduct above the head or pull too far laterally [21].

Neurapraxia can manifest itself as numbness, pain, tingling burning, weakness or paralysis. The motor or sensory dysfunction is temporary with function returning in 6–8 weeks. Once recognised, neurapraxia should be treated with physical therapy to speed functional recovery.

15.3 Renal Vascular Complications

15.3.1 Haematoma

Retroperitoneal and perinephric haematomas can be the result of either continuous venous oozing or a brisk arterial bleed from a vessel previously in spasm. Small perinephric haematomas are common and for the most part have little clinical implications, while a larger haematoma can lead to complications and prolonged hospitalisation following PN. Haematomas, if large enough, may cause ileus, become infected or cause haemodynamic instability. Conservative

management is the mainstay of treatment for most perinephric haematomas reserving intervention for select cases. Vigilant monitoring of haemoglobin is indicated in all patients and blood transfusions used for patients with signs of continued blood loss. Selective arterial embolisation is reserved for patients with continuous bleeding. If angiographic embolisation is unsuccessful or the patient is haemodynamically unstable, re-exploration should not be delayed. Prevention of a retroperitoneal haematoma is achieved by meticulous haemostasis at the conclusion of the procedure. Particular attention should be paid in patients that are hypovolaemic or in the case of vasoconstrictor administration; both these factors can potentially mask bleeding vessels.

15.3.2 Bleeding

Intraoperative bleeding from the cut edge of renal parenchyma is a factor complicating PN. A large multi-institutional analysis reported an intraoperative haemorrhage rate of 1.0% during RAPN [16]. A systematic and routine approach to PN will minimise incidence of intraoperative haemorrhage. A clear understanding of renal vascular anatomy will help with surgical planning. Contrasted CT scan of the abdomen will help identify renal hilar vasculature aiding in the surgeon's approach. The number of arteries and veins supplying the kidney should be noted in every patient, guiding surgical dissection of the renal hilum. After the vascular clamps are placed to produce renal ischaemia, bleeding may still be encountered. An unrecognised or anomalous renal artery can cause unexpected bleeding during tumour resection after clamping. If one is not expeditious in isolating the suspected artery, a cross clamp of the entire renal hilum can be employed to control the vessel. Alternatively, in cases where renal artery and vein have both been clamped, brisk bleeding may be from obstructed venous outflow of the kidney. In this case the surgeon should attempt to release the clamp from the vein, leaving the arterial clamp in place, to help the bleeding subside.

If continuous bleeding is experienced during the immediate postoperative days, blood transfusion is warranted. Signs of persistent bleeding after multiple transfusions should trigger one to proceed with angiography and selective arterial embolisation. Exploratory surgery for a bleeding patient usually results in nephrectomy.

15.3.3 Pseudoaneurysm and Arteriovenous Fistula

Patients may present with delayed bleeding, which is typically caused by a pseudoaneurysm or arteriovenous fistula, although rare. Reported rates of pseudoaneurysm and arteriovenous fistula are 2.0% after minimally invasive PN [22]. If pseudoaneurysm or arteriovenous fistula is suspected, angiography should be performed. When pseudoaneurysm or fistula is diagnosed, selective embolisation is a very effective treatment.

15.3.4 Infarction

The role of PN is to remove the renal mass while preserving as many nephrons as possible. Infarction of the renal parenchyma after resection not only undermines the goal of nephron-sparing surgery but also lends one to a higher risk of developing a urine leak after surgery. To avoid infarction it is important to resect the tumour while minimising the margin of normal renal parenchyma. The more proximally an artery is transected, the broader the infarction zone of renal parenchyma will be. Minimising renal parenchymal excision will help minimise transection of renal arterial supply, thereby minimising the infarction zone.

One should recognise that renorrhaphy technique also plays an important part to either cause or prevent renal parenchymal infarction. The surgeon should be mindful that wide and deep placement of suture into the renal parenchyma, though sometimes necessary, has the potential to

constrict segmental arteries causing infarction to zones of the kidney not involved in resection.

Management of renal infarction after PN is conservative and consists of observation. Note that the true significance or renal infarction is unknown. However, it is theorised that large infarction can lead to renin-mediated hypertension [23]. Nephrectomy is indicated in patients found to have severe renin-mediated hypertension caused by infarcted renal tissue.

15.4 Collecting System Complications

Urine leak can occur after thermal ablative therapy and PN. During thermal ablative procedures, urine leak is a consequence of either direct puncture of the collecting system or involvement of the collecting system in the ablation zone. Ureteropelvic junction obstruction, occurring in 1.1–2.4% of thermal ablation cases [1, 24], puts one at higher risk of developing a urine leak or will exacerbate an existing leak. Hence thermal ablative therapy is contraindicated in those patients with a tumour abutting the ureteropelvic junction. The incidence of urine leak after renal cryoablation is 1.2–3.2% [25, 26].

Unrecognised violation of the collecting system is often the cause of urine leaks after PN. Closure of the defect with absorbable sutures is important and will help prevent urinary leakage. The rate of urinary leak after RAPN is reported to be between 0.6 and 2% [7, 13, 16, 27–29].

Treatment of urine leak is based on three principles: [1] adequate drainage, [2] unobstructed distal flow of urine and [3] treatment or prevention of infection. Drain placement into a retroperitoneal urinoma adjacent to the kidney is necessary in symptomatic or infected urine collections. The drain should remain in place until the leak resolves. If ureteral obstruction is evident, placement of a stent is justified. A Foley catheter should be placed to decompress the bladder, particularly in patients with high voiding pressure, to prevent reflux and thus further leakage of urine. In the absence of ureteral obstruction, a stent is unnecessary. An adequately drained urine collection will prevent infection in patients with low risk for infection. Patients with high risk of infection should be treated with prophylactic antibiotics while the drain is in place.

15.5 Injury to Abdominal Structures

Renal surgery requires a thorough understanding of abdominal anatomy. Nearly any abdominal structure may be encountered through the course of a particular surgery. The right kidney is in immediate proximity to the liver, gallbladder, ascending colon and the duodenum. Structures surrounding the left kidney include the spleen, tail of the pancreas and descending colon. The close proximity of these organs imparts a risk of injury during surgery. Injuries associated with gaining laparoscopic access to the peritoneum have also been recognised. Vascular injuries to the great vessels, mesentery, omentum and pelvic vasculature have all been reported as well as injuries to small and large bowel. Diaphragm and pleural injury is another complication not to be forgotten in renal surgery.

15.5.1 Hepatobiliary

The most common injury to the liver is attributed to thermal injury from cautery. Lacerations of the liver parenchyma occur more rarely from overzealous retraction. Thermal injuries require no intraoperative intervention. Intervention of a hepatic laceration should be initiated if it causes significant haemorrhage. In this case electrocautery or argon beam coagulation supplemented with haemostatic agents will usually suffice. If the laceration is large enough and a bile leak is suspected, placement of a drain is warranted. In the case of injury to the gallbladder, cholecystectomy should be performed with the aid of a general surgeon.

15.5.2 Spleen

Splenic injury is overwhelmingly caused by vigorous traction on the splenic ligaments causing the splenic capsule to tear. Contemporary literature sites a splenic injury rate 1.3–24% during left-sided renal surgery [30]. Splenic injury as a result RAPN is reported to be less than 1% [7, 18]. Prevention of tears is best achieved by meticulous dissection and release of the splenic ligaments prior to placing undue traction and proceeding to the superior pole kidney. Attempts may be made to ameliorate the bleeding by use of argon beam coagulation combined with haemostatic agents and compression. If efforts to stop bleeding are futile, proceeding with splenectomy is justified. In splenectomised patients postoperative vaccination for encapsulated organisms (*Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*) is necessary.

15.5.3 Bowel

Bowel injury is a rare complication arising from thermal injury, arc from electrocautery or difficult dissection. Previous abdominal surgery and intense perinephric inflammatory reaction are factors leading to increased rates of bowel injury. Close attention must be paid during dissection and manipulation of bowel. A missed bowel injury can be a catastrophic postoperative complication. Small sharp lacerations can be closed primarily in two layers and reinforced with omentum when possible. Larger lacerations or those recognised postoperatively require a formal resection with anastomosis and should take place with the help of a general surgeon. In the case of unanticipated intestinal spillage into the abdominal cavity, one should copiously irrigate the cavity with warmed saline. After unanticipated colonic content spillage, a drain should be placed in the cavity, and antibiotics covering gram-negative and anaerobic organisms should be added for prophylaxis. Nasogastric tube decompression is recommended until return of bowel function ensues. Rate of bowel injury from RPN and LPN is 0.25% and 0.31%, respectively [18]. Bowel injury as a result of cryoablation was found to be 1.1–2.7% [31, 32].

15.5.4 Pancreas

Pancreatic injury is rare and occurs more frequently as a complication of left-sided renal surgery. Pancreatic injury during laparoscopic left-sided renal surgery was found to be 0.4% [33]. However, this was during radical nephrectomy or adrenalectomy. Injury is a consequence of direct laceration or forceful retraction. It may be prevented by early identification and careful dissection of the pancreas when working near the left renal hilum. Capsular injuries are managed by closure of the capsule with non-absorbable suture. A pancreatic fluid leak may occur if the injury is extensive and involves the pancreatic duct. Pancreatic resection distal to any ductal injury is most often necessary. Use of a gastrointestinal stapler is an effective means for transection and ligation of the distal pancreas after pancreatic ductal injury requiring resection [33]. General surgery consultation should be triggered to aid in the repair of pancreatic injuries. A drain should be placed to prevent collection of leaked pancreatic juices. Nasogastric tube decompression is advised in the immediate postoperative period. Monitoring for signs and symptoms of pancreatitis, including serum amylase and lipase levels, will aid with postoperative management. If severe pancreatitis presents, parenteral alimentation must be initiated, and abdominal cross-sectional imaging should be used to evaluate for pancreatic necrosis.

15.5.5 Vascular

Vascular injury is a relatively common complication of renal surgery. The injury often occurs from laparoscopic access or dissection injury. Abdominal wall vessels are often injured as a consequence of laparoscopic trocar placement. Abdominal wall vessel injury, when recognised, is controlled by manipulation of the trocar to tamponade the bleeding until repair is completed.

Suture ligation of the injury is completed using a Carter-Thomason needle. If this method is unsuccessful, direct cut down to the vessel and ligation is warranted.

Control of vascular injury in laparoscopy is complicated by the exclusion of direct manual or digital pressure. It is important the surgeon quickly and carefully assesses the damage to determine if the injury can be managed laparoscopically or should be converted to open surgery. Pressure can be held gently with an atraumatic instrument to control bleeding while the surgeon assesses the situation. Proximal and distal dissection is important to visualise and safely control the bleeding vessel. Once identified ligation with sutures, clips or staples may be employed.

In the situation wherein the surgeon believes judicious laparoscopic repair is not possible, conversion to open or hand-assisted surgery should not be delayed. An open surgical set should always be immediately available during laparoscopy. Direct pressure, if possible, and pneumoperitoneum are maintained until the table is prepared for open surgery.

15.5.6 Diaphragm

Diaphragmatic and pleural injury occurs from flank incisions at the 11th rib level and superiorly. During laparoscopic surgery, the diaphragm is injured during mobilisation of the spleen, liver or colon and also by dissection of the superior pole kidney. Pleural injury at time open partial nephrectomy (OPN) was reported to be 11.5% [34]. Pleural injury and pneumothorax during laparoscopic renal surgery are reported at 0.75% [35]. A small pleurotomy should be managed at the conclusion of the operation by insertion of a red rubber catheter into the thorax through the pleurotomy and a non-absorbable suture used to place a purse-string stitch around the pleurotomy. The anaesthetist is asked to give the patient a deep inspiration and held, the catheter is removed and the suture tied to occlude the defect. When the injury is made during laparoscopy, a skilled surgeon may repair the defect without conversion to open surgery. Chest radiographs postoperatively are helpful in evaluating for pneumothorax. A small pneumothorax can be managed conservatively with oxygen supplementation and respiratory therapy. Avoid positive pressure breathing treatments in patients with pneumothorax as such treatment may cause or exacerbate a pulmonary air leak. More extensive pneumothorax should be managed with a thoracostomy tube and monitoring with chest radiographs to ensure resolution before removal of the thoracostomy tube.

15.6 Acute Renal Insufficiency

Acute renal insufficiency in nephron-sparing surgery is most common in patients with imperative indications: solitary kidney, bilateral tumours or compromised renal function. Multiple studies have shown excellent long-term renal functional preservation following nephron-sparing surgery. Kim et al. reported a 6.2% incidence of new onset CKD after PN [36]. Others have shown a 20.2% CKD upstaging, by one class or more, of pre-existing CKD after PN [35]. However, due to acute changes in the normal renal parenchyma following nephron-sparing surgery, acute renal failure can be an unfortunate complication in the immediate postoperative period.

Thermal ablation can cause acute renal insufficiency by destruction of nephrons from extension of the ablation zone outside the tumour margin. The ablation zone, in theory, is capable of creating infarction by affecting vessels supplying normal renal parenchyma. Rates of acute renal insufficiency from thermal ablation are poorly reported.

Acute renal insufficiency after PN is caused by acute tubular necrosis from global renal ischaemia. Objective data to report mild cases of acute renal insufficiency, oliguria or change in eGFR is generally poorly defined or reported. However, the incidence of severe acute renal insufficiency requiring dialysis after PN is 0.2–0.9% [9, 16, 29, 37].

Multiple methods exist to reduce ischaemic damage to the nephron thereby decreasing inci-

dence of acute renal insufficiency. Techniques usually focus on either decreasing ischaemia time or reducing the damage imparted by decreased blood flow to the renal parenchyma. Methods to reduce ischaemia time include early unclamping of the renal hilum [38]. This allows a shorter ischaemia time; however, the renorrhaphy must then be completed in the presence of increased bleeding. Another technique less commonly used in open surgery is manual compression of the kidney to compress parenchymal vessels while excising the tumour allowing the remainder of the kidney perfusion. Mannitol administration prior to arterial clamping and just after unclamping is a method to increase renal blood flow and is believed to scavenge free oxygen radicals in the ischaemic renal tissue, reducing oxidative stress [39]. Another method shown to reduce nephron injury during renal ischaemia is renal cooling with ice slurry.

Treatment of acute renal insufficiency in the postoperative setting consists of minimising further renal insults. Avoid hypotension and hypovolemia; withhold nephrotoxic medications such as aminoglycosides, NSAIDS, ACE inhibitors and IV contrast agents. In severe cases of acute renal insufficiency, temporary dialysis may be required.

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