Renal cell carcinoma: modern surgical approach
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Purpose of review
In the past decade, minimally invasive therapy options for renal cell carcinoma have been devised in an attempt to minimize operative morbidity while achieving comparable oncologic and functional outcomes. Herein, we evaluate the new developments related to the modern surgical and energy ablative techniques for renal cell carcinoma.

Recent findings
When compared with the open counterpart, laparoscopic radical and partial nephrectomies have equivalent operative time, decreased blood loss, superior recovery, and improved cosmesis. Nowadays, laparoscopic radical nephrectomy can be performed for pT2 tumors (up to 15 cm), and level I renal vein thrombus is not a formal contraindication for the laparoscopic procedure. Ongoing advances in laparoscopic techniques and operator skills have allowed the development of a reliable technique of laparoscopic partial nephrectomy, which includes the ability to achieve effective intracorporeal renal hypothermia. Cryoablation and radiofrequency ablation therapies have been performed through a laparoscopic or percutaneous approach, using a combination of fine probes and high-resolution imaging studies to precisely target the lesions and accurately monitor the freezing or heating ablation process. Noninvasive tumor ablation can now be achieved by extracorporeally induced high-intensity focused ultrasound.

Summary
These minimally invasive techniques represent the modern surgical approach for renal cell carcinoma, aiming to decrease patient morbidity. Laparoscopic radical and partial nephrectomy techniques duplicate the open approach. Results obtained with energy ablative techniques are encouraging. Based on the known slow growth rates of small renal cell carcinoma, one should be cautious when interpreting the short-term results of energy ablative therapies monitored by imaging only.

Keywords
laparoscopy, partial nephrectomy, radical nephrectomy, cryoablation, radiofrequency ablation, high-intensity focused ultrasound

Abbreviations
HIFU high-intensity focused ultrasound
RCC renal cell carcinoma

Introduction
In the past decade, several minimally invasive therapy options for renal cell carcinoma (RCC) have been devised in an attempt to minimize operative morbidity while achieving comparable oncologic and functional outcomes [1–3,4**]. These minimally invasive procedures comprise surgical ablative techniques (laparoscopic radical and partial nephrectomy), which aim to duplicate the established open surgical principles, and energy ablative techniques (cryoablation, radiofrequency ablation, high-intensity focused ultrasound), which use energy sources while leaving the thermo ablated tissue in situ [5–7].

Laparoscopic radical nephrectomy is now an established procedure for management of indicated patients with localized tumors [8,9]. Current data indicate that, compared with the open approach, the laparoscopic procedure is associated with comparable operative time, decreased blood loss, superior recovery, improved cosmesis, and equivalent cancer control over an intermediate and long-term follow-up [10,11**]. Laparoscopic partial nephrectomy is emerging as an attractive minimally invasive nephron-sparing option at select institutions. Ongoing advances in laparoscopic techniques and operator skills have allowed the development of a reliable technique that replicates all the steps of the open counterpart [12].

Cryoablation and radiofrequency ablation therapies have been used during nephron-sparing surgery, following the growing tendency to preserve the affected kidney while minimizing patient morbidity. These procedures have been performed through a percutaneous approach, using a combination of fine probes and high-resolution imaging studies to precisely target the lesions and accurately monitor the freezing or heating ablation process [5,6]. Taking the last step on the succession ‘from knife to needle to nothing’, noninvasive tumor ablation can now be achieved by extracorporeally induced high-intensity focused ultrasound (HIFU) [7].

In this review article, we evaluate the new developments related to the modern surgical and energy ablative techniques for RCC.
Laparoscopic radical nephrectomy

Nowadays, laparoscopic radical nephrectomy can be performed for most patients with organ-confined T1–T3aN0M0 renal tumors [13]. It is important to highlight that this minimally invasive approach should only be offered to patients that are not candidates for nephron-sparing surgery. Recently, Matin et al. [14] compared the outcome of laparoscopic radical and open partial nephrectomy for the sporadic renal tumor, 4 cm or smaller, with a normal contralateral kidney. The authors concluded that the significant short and intermediate-term benefits of the laparoscopic (radical) approach in these circumstances must be weighed against its long-term disadvantages, such as the possibility of a new contra-lateral tumor or the development of chronic renal insufficiency.

Circumstances that were previously considered relative contra-indications for laparoscopic radical nephrectomy, such as larger tumors and tumors with level I renal vein thrombus, are now amenable to this minimally invasive approach. We believe that tumors as large as 15 cm are suitable for laparoscopic excision, however this decision needs to be made based on the experience of the individual surgeon. Steinberg et al. [15] reviewed the overall experience of the Cleveland Clinic, where 33 of 300 laparoscopic radical nephrectomies were carried out on larger, clinical stage T2 tumors, 7 cm or greater in size. Mean tumor size was 9.8 cm, with 17 tumors between 7 and 10 cm and 16 tumors over 10 cm. This group was compared with a contemporary group of 34 patients undergoing open radical nephrectomy for tumors larger than 7 cm in size. Tumors over 14 cm or with inferior vena cava (IVC) thrombus were excluded from this study. Estimated blood loss (laparoscopy, 294 cm³; open, 837 cm³; P<0.001) and hospital stay (laparoscopy, 1.8 days; open, 6.1; P<0.001) were reduced in the laparoscopic group. Although there was a trend towards less surgical complications in the laparoscopic group, this finding was not statistically significant (6.2% versus 23.5%; P=0.08).

Recently, Desai et al. [16] reported a series of eight patients who underwent laparoscopic radical nephrectomy in the presence of gross tumor involvement of the renal vein identified on preoperative computed tomography scan. In this group of patients, mean tumor size was 12.4 cm (6–20 cm). All procedures were successfully completed laparoscopically, except for one open conversion due to intraoperative hemorrhage (1000 ml). After the renal artery was clipped and transected, the renal vein was dissected proximally towards the inferior vena cava. While the renal vein segment containing the thrombus clearly appeared full and bulky, the uninvolved, free-of-thrombus proximal renal vein segment was flat on laparoscopic examination. This established a clear line of demarcation, where the articulating endoscopic gastrointestinal anastomoses stapler was safely fired. Intraoperative laparoscopic ultrasonography with color Doppler is helpful to precisely delineate the proximal extent of the thrombus and should be used routinely.

Laparoscopic radical nephrectomy has proved to be a safe procedure with a low incidence of complications in the hands of urologists with reasonable experience in minimally invasive techniques. Siqueira et al. [17] reviewed the Indianapolis experience of major surgical complications in laparoscopic nephrectomy (61 radical nephrectomies). The authors reported an incidence of 4% of major complications including one vascular complication – division of a superior mesenteric artery, which required open surgical revascularization, but unfortunately resulted in the patient’s death; one hemorrhagic complication – inadvertent transaction of an aberrant right lower pole artery, which required conversion to open surgery for its control; one visceral complication – liver laceration during port placement, which was managed laparoscopically with oxidize cellulose packing; one bowel complication – semi-circumferential ischemic lesion at the splenic flexure of the colon, for which no further intervention was required. The authors reinforced the importance of a thorough pre-operative imaging evaluation to rule out renal vascular variants. If accurate preoperative imaging studies are not available, it would be prudent for the surgeon, after clipping and incising the main renal artery, to proceed with careful dissection of the medial aspect of the upper and lower pole of the kidney to avoid any uncontrolled aberrant accessory vessel division. They also stress that large hilar tumors distorting the renal hilum deserve special attention to avoid transection of any aberrant major aortic branch (superior mesenteric artery).

To achieve optimal oncologic outcomes, established principles of renal cancer surgery must be respected. The excised surgical specimen must be removed in a hermetic sac to avoid contact with the abdominal wall [18,19]. Either intact specimen extraction or morcellation are safe with regard to oncological outcomes [20]. Nonetheless, one must be careful to avoid the rare complication of sack perforation with potential tumor spillage during morcellation. In the aggregate, laparoscopic radical nephrectomy does not result in an increased risk of port site seeding, local recurrence or metastasis. Recently, Tsivian and Sidi [18] reported a comprehensive review of experimental and clinical studies focused on port site metastases. The authors found three cases of port site metastases following laparoscopic radical nephrectomy for RCC and suggested a few preventive steps: avoid laparoscopic surgery in the presence of ascites; the trocar should be fixed to prevent...
dislodgement; avoid gas leakage around the trocar; adequate surgical technique, minimal handling and avoiding tumor boundary violation; use of an impermeable bag for specimen removal. The authors highlight that the role of morcellation in the pathogenesis of port-site metastases remains controversial. Nevertheless, two out of the total three reported cases of RCC port-site seeding occurred following specimen morcellation [21,22].

Our routine practice for extraction of the cancerous specimen aims to provide an intact specimen for accurate pathologic staging while achieving a superior cosmetic result [20]. Valuable histopathologic information regarding tumor stage and completeness of tumor resection with negative surgical margins cannot be reliably obtained following specimen morcellation [13]. Currently, we routinely perform intact specimen extraction through a low muscle-splitting Pfannensteil incision in male patients and through the vagina in female patients [23,24]. This approach removes any practical cosmetic disadvantage to our philosophy of intact extraction, while maintaining oncological sanctity of the intact pathologic specimen. We recently reported the detailed technique and results of transvaginal extraction of the intact laparoscopic radical nephrectomy specimen in 10 patients [24]. Median operative time for the vaginal extraction procedure was 35 min with minimal blood loss. Median tumor size was 3.6 cm (range from 2.4 to 7.4) and median specimen weight was 327 g (range 152–484). Postoperative questionnaires revealed excellent patient satisfaction and convalescence.

Long-term oncological data on laparoscopic radical nephrectomy are still sparse. Portis et al. [11**] reviewed the experience of three centers where 64 patients were treated laparoscopically before November 1996. These patients were compared with an open cohort of 69 patients treated with open radical nephrectomy. On preoperative imaging open lesions were larger (6.2 cm) than the laparoscopic radical nephrectomy lesions (4.3; \( P<0.001 \)). Pathology revealed no difference in average Fuhrman grade (1.88 and 1.78; \( P=0.476 \)). The median follow-up was 54 months for laparoscopy and 69 months for open radical nephrectomy. Kaplan-Meier analysis with log rank comparison revealed 5-year recurrence-free survival of 92% and 91% for laparoscopic and open radical nephrectomy, respectively. At 5 years cancer specific survival was 98% and 92% (\( P=0.124 \)) for laparoscopic and open radical nephrectomy, respectively. Thereafter, the authors concluded that laparoscopic radical nephrectomy confers long-term oncological effectiveness equivalent to traditional open radical nephrectomy [11**].

## Laparoscopic partial nephrectomy

Laparoscopic partial nephrectomy was initially reserved for the select patient with a favorably located, small, peripheral, superficial, exophytic tumor [25–27]. At the Cleveland Clinic, we have developed a reliable technique for laparoscopic partial nephrectomy that allows us to carefully expand our indications to include select patients with more complex tumors: patients with a tumor deeply invading the parenchyma up to the collecting system or renal sinus; a completely intrarenal tumor; a tumor abutting the renal hilum; a tumor in a solitary kidney; or a tumor substantial enough to require hemi-nephrectomy [4**,12]. Nonetheless, laparoscopic partial nephrectomy is an advanced and challenging procedure that involves significant issues such as securing renal hypothermia, renal parenchymal hemo-tasis, pelvicalyceal reconstruction, and parenchymal renorrhaphy.

Our technique of laparoscopic partial nephrectomy addresses these technical difficulties by duplicating the principles of the open partial nephrectomy. This technique has been recently described based on our initial experience with 50 patients [4**]. A ureteral catheter is inserted cystoscopically up to the renal pelvis. Transperitoneally, access preferred for anterior, lateral, and upper-pole tumors, a Satinsky clamp is used to occlude the renal hilum en bloc. Retropertioneoscopically, access preferred for posterior, and posterior-laterally located tumors, the renal artery and vein are dissected separately for individual placement of bulldog clamps. Laparoscopic ultrasonography precisely delineates tumor size and intraparenchymal extension, guiding the surgeon to score the proposed line of resection with an adequate margin of normal renal parenchyma. The hilum is clamped, and the tumor is excised and entrapped within an Endocatch bag. Injection of dilute indigo carmine through the ureteral catheter identifies any pelvicalyceal entry, which is suture repaired by intracorporeal laparoscopic techniques. Finally, the renal parenchyma is reconstructed using 0 vicryl suture over prefashioned surgical bolsters to complete a hemostatic renorrhaphy.

We believe that transient hilar clamping is an important prerequisite for a technically superior laparoscopic partial nephrectomy [4**,12]. Nonetheless, the infrequent, small, completely exophytic tumor may be resected without hilar control. Recently, Guillonneau and colleagues [28*] compared the outcomes of laparoscopic partial nephrectomy with (group I, 12 patients) and without (group II, 16 patients) clamping techniques of the renal vasculature. The authors reported a mean laparoscopic operating time of 179 min in group I compared with 121 min in group II (\( P=0.004 \)). A significantly higher intraoperative blood loss was reported in the patients.
without hilar clamping (708 ± 569 versus 270 ± 281 ml; \( P = 0.014 \)). Three patients in group I and two in group II required blood transfusion. Surgical margins were negative in all specimens. The authors acknowledge that bipolar cautery or ultrasonic shears may provide hemostasis without renal vascular control [29]. These modalities of hemostasis char the tissue, however, resulting in poor visualization of tumor margins. The authors report that the main advantage of renal vascular clamping is the quality of visualization of the renal parenchyma, allowing good observation of the tumor mass and surgical margins, which helps in accurate tumor excision. In this study, Guillonneau et al. also reported the use of continuous pelviccalyceal irrigation with cold saline during renal vascular clamping (mean renal ischemia time of 27.3 min, ranging from 15 to 47 min) in an effort to decrease renal insult due to ischemia [28*,30].

During open partial nephrectomy, surface cooling of the kidney with ice slush is the technique of choice for achieving renal hypothermia [31–33]. We recently described a technique of intracorporeal ice-slush renal hypothermia for laparoscopic partial nephrectomy, thus replicating the open approach [34*•]. Twelve selected patients with an infiltrating renal tumor who were candidates for nephron-sparing surgery underwent transperitoneal laparoscopic partial nephrectomy with renal hypothermia. Median tumor size was 3.2 cm (range 1.5–5.5 cm), six tumors (50%) were central in location, and an imperative indication for partial nephrectomy was present in seven patients (58%), including two patients (17%) who had a tumor in a solitary kidney. An Endocatch-II bag was placed around the mobilized kidney, and its drawstring cinched around the intact renal hilum. The renal artery and vein were occluded with a Satinsky clamp. Five 30 cm³ syringes were previously modified by cutting off the nozzle-end of the barrel, and prefilled with ice-slush in preparation for rapid injection. The bottom of the engaged bag was retrieved through a 12 mm port site, opened, and ice-slush was introduced within the bag to completely surround the kidney. After renal hypothermia was achieved, laparoscopic partial nephrectomy was performed using our standard technique. All procedures were successfully completed laparoscopically without open conversion. Median time to deploy the bag around the kidney was 7 min (range 5–20 min), median volume of ice-slush introduced was 600 cm³ (range 300–750 cm³), and mean time taken to insert the ice-slush was 4 min (range 3–10 min). A nadir renal parenchymal temperature ranging from 5 to 19.1°C was achieved in the five patients in whom thermocouple measurements were performed. In three patients serial thermocouple measurements were obtained; terminal renal parenchymal temperatures at completion of partial nephrectomy, just prior to hilar unclamping, were 19, 19.5, and 23.8°C following 43, 48, and 44 min of ischemia, respectively. These data provide assurance that adequate renal hypothermia which lasts for the duration of hilar clamping can be achieved by this technique.

**Cryoablation**

During cryoablation, the targeted tissue is rapidly frozen *in situ*, which is followed by sloughing of the devitalized tissue and healing by secondary intention over time. Cryotherapy-induced cytotoxic necrosis includes rapid intracellular ice formation and delayed microcirculatory failure [5,35*,36]. Initially, freezing of the extracellular matrix is followed by rapid intracellular freezing, a lethal event, leading to cell membrane dysfunction and cellular disruption. Secondarily, delayed microcirculatory failure occurs during the thaw phase of the freeze–thaw cycle, consisting of vasoconstriction, endothelial damage, microvascular thrombosis and, ultimately, cessation of blood flow. The lethal temperature for achieving reliable deaths of normal and cancerous renal cells is in the vicinity of −40°C [5].

Cryoenergy has been the most studied energy source for ablation of renal tumors. Nowadays it represents a viable option for treatment of small peripheral renal masses. It can be delivered either laparoscopically or percutaneously. Lee and colleagues [35*] reported their experience with 20 patients who underwent retroperitoneal laparoscopic cryoablation for small renal masses (1.4–4.5 cm), using a double-freeze technique. Needle biopsies of solid masses were performed intraoperatively, revealing RCC in 11 patients. Of these 11 patients, none had evidence of recurrent disease at last follow-up, with scans showing no enhancement of any lesions. Of eight patients with follow-up of 2 years or greater, four had complete resolution of renal lesions (50%). The remainder had lesions that were reduced or stable in size.

Patients with von Hippel-Lindau disease face the prospect of multiple open surgical procedures with associated morbidity and long convalescence. Recently, Shingleton and Sewell [36] reported their initial experience with percutaneous renal cryoablation for patients with this condition. A total of five tumors (2.8–5 cm) in four patients were treated. An interventional magnetic resonance imaging unit was used for probe (2 or 3 mm) guidance and ice ball monitoring. Patients were hospitalized overnight for observation and discharged home the following day. Two patients required re-treatment due to residual tumor. At follow-up, ranging from 2 to 23 months, there was no radiographic evidence of recurrence.

**Radiofrequency ablation**

Radiofrequency ablation provides heat-based tissue destruction [6,37*•]. High-frequency electrical current
creates molecular friction, denaturation of cellular protein, and cell membrane disintegration. The threshold temperature necessary for tissue thermal destruction is in the range of 40–70°C. Radiofrequency tumor ablation can be performed using either the ‘dry’ or ‘wet’ technique. Infusion of hypertonic saline in the ‘wet’ technique promotes centrifugal dissipation of radiofrequency energy, resulting in rapid creation of larger radiolesions, without the early tissue desiccation noted during the ‘dry’ procedure [6,37**].

Recently, Rendon and colleagues [37**] reported their findings on immediate and delayed nephrectomy following radiofrequency ablation of RCC in 10 patients (11 masses). All masses were biopsied before treatment. In four patients, five RCCs were treated with radiofrequency after surgical exposure of the tumor followed immediately by partial or radical nephrectomy (acute group). Six other patients were treated percutaneously with ultrasound or computed tomography guidance under local anesthesia and intravenous sedation 7 days before partial or radical nephrectomy (delayed group). Pathological examination demonstrated residual viable tumor in approximately 5% of the volume in four of the five tumors in the acute group and in three of the six masses in the delayed group. In one delayed case the viable tumor appeared to be in contact with the renal vein. The authors express their concerns about the uncertainty of radiofrequency ablation. Moreover, based on the known slow growth rates of small RCCs, they warn that short-term results of thermal therapy monitored by imaging only should be interpreted with caution.

High-intensity focused ultrasound ablation

HIFU has the potential to be the least invasive of tumor ablative techniques [7,38*]. HIFU employs beams of ablative ultrasound frequency generated by a cylindrical piezoelectric element focused by a paraboloid reflector. Similar to extracorporeal shockwave lithotripsy, this beam is then focused on the lesion at F2. Thermal destruction results, as evidenced on pathology by localized hemorrhage, coagulative necrosis, and chronic inflammatory infiltration.

Most of the literature related to HIFU performed for renal tumors has only been experimental in nature. Recently, Kohrmann and colleagues [38*] reported specific details on a patient with RCC (three lesions) who underwent HIFU (three sessions) with curative intent. After treatment, magnetic resonance imaging showed necrosis in the two tumors located in the lower pole of the kidney in approximately 5% of the volume in four of the five tumors in the acute group and in three of the six masses in the delayed group. In one delayed case the viable tumor appeared to be in contact with the renal vein. The authors express their concerns about the uncertainty of radiofrequency ablation. Moreover, based on the known slow growth rates of small RCCs, they warn that short-term results of thermal therapy monitored by imaging only should be interpreted with caution.

ultrasound energy by the interposed ribs. General anesthesia was required to apply high energy levels of focused ultrasound [38*].

Conclusion

Minimally invasive techniques (laparoscopic radical and partial nephrectomy) represent the modern surgical approach for RCC. These techniques replicate the safety and efficacy of the traditional open approach while significantly decreasing patient morbidity. Preliminary results with energy ablative techniques are encouraging, but require long-term follow-up to prove their efficacy.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

* of special interest
** of outstanding interest

11 Portis AJ, Yan Y, Landman J. Long-term follow-up after laparoscopic radical nephrectomy. J Urol 2002; 167:1257–1262. This is the first report on long-term follow-up after laparoscopic radical nephrectomy. These data confirm the oncologic adequacy of the laparoscopic approach for RCC.
Kidney, testis and penile cancer

An excellent review of surgical complications following laparoscopic kidney surgery, which reinforces the safety of this minimally invasive approach.

A thorough review on risk factors for port site metastasis during urological laparoscopic surgery. The authors highlight that two out of three cases of RCC port site metastasis occurred following specimen morcellation.


This paper describes a technique for intact specimen extraction while achieving superior cosmetic results.


This paper outlines the importance of renal hilar vessels control during laparoscopic partial nephrectomy.


An elegant description of the laparoscopic technique of renal hypothermia for partial nephrectomy. This technique may extend the scope of laparoscopic partial nephrectomy to more complex cases.

This paper shows that the renal cryolesion is completely reabsorbed in 50% of the patients followed for at least 2 years.


This paper highlights that, based on the known slow growth rates of small RCC, one should interpret the short-term results of thermal therapy monitored by imaging only with caution.

This paper shows that adequate delivery of high energy levels of focused ultrasound requires general anesthesia and may be precluded by the interposed ribs.
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