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Laparoscopic Partial Nephrectomy – Current State of the Art

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1. Introduction

Clayman et al described the first successful laparoscopic nephrectomy in 1991 [1]. Since that time, laparoscopic radical nephrectomy has become the standard of care for renal tumors. At the same time, the widespread use of contemporary imaging techniques has resulted in an increased detection of small incidental renal tumors. In efforts to avoid chronic kidney disease, the management of the small renal mass has trended away from radical nephrectomy toward nephron-conserving surgery. In 1993, successful laparoscopic partial nephrectomy (LPN) was first reported in a porcine model [2]. Winfield et al reported the first human LPN in 1993 [3]. From that time, centres around the world have developed laparoscopic techniques for partial nephrectomy through retroperitoneal and transperitoneal approaches. Classically, only small, peripheral, exophytic tumors were eligible for LPN, but larger, infiltrating tumors have been managed with LPN in more recent series [4].

Currently, partial nephrectomy is a standard of care treatment for the surgical management of localized renal tumors <4cm [5], and recommended in guidelines published by the American Urological Association [6] and European Association of Urology [7]. LPN combines the benefits of nephron-sparing surgery and laparoscopy to decrease the morbidity of partial nephrectomy.

The LPN technique has evolved significantly over the past decade such that its safety and efficacy rival those of open partial nephrectomy (OPN) and laparoscopic radical nephrectomy (LRN) techniques for tumors less than 4cm. LPN produces low overall morbidity, faster post-operative recovery, and comparable oncologic outcomes compared to other techniques.

Technical difficulty in LPN is encountered when securing renal hypothermia, renal parenchymal hemostasis, pelvicalyceal reconstruction, and parenchymal renorrhaphy by pure laparoscopic techniques. The appropriate and optimal length of warm ischemia time (WIT) remains particularly controversial. Nevertheless, ongoing advances in laparoscopic techniques and operator skills have allowed the development of a reliable technique that duplicates the established principles and technical steps underpinning open partial nephrectomy. With the advent of the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), robot-assisted LPN (RPN) has advanced laparoscopic techniques even further. In this chapter we evaluate the role of LPN in the nephron-sparing armamentarium.

2.1 Indications and contraindications

Partial nephrectomy is performed for benign and malignant renal conditions. In the setting of malignant renal diseases, this is indicated in situations where radical nephrectomy would leave the patient anephric due to bilateral renal tumors or unilateral tumor and compromised or at risk the other side. Some investigators also defined the role of elective PN in patients with unilateral renal tumors and normal contralateral kidneys to reduce the risk of developing chronic kidney disease in the future [8].

Due to its technical limitations, LPN was initially reserved for select patients with small, peripheral, superficial, superficial, and exophytic tumors. As laparoscopic experience increased, the use of LPN was expanded to technically challenging tumors, such as tumors invading deeply into the parenchyma up to the collecting system or renal sinus, intrarenal tumors, tumors abutting the renal hilum, tumors in solitary kidneys, or tumors substantial enough to require heminephrectomies. Recent series include larger, Stage T1b tumours [9-11]; endophytic tumours near the hilum and upper pole [12]; bilateral tumors [13]; multiple ipsilateral tumors [14]; and stage T1a tumours presenting in select patients over the age of 70 [15].

General contraindications to abdominal laparoscopic surgery are applied to LPN. Specific absolute contraindications to LPN include bleeding diathesis (such as renal failure induced platelet dysfunction and blood thinners), renal vein thrombus, and aggressive locally advanced disease. Morbid obesity and a history of prior renal surgery may prohibitively increase the technical complexity of the procedure and should be considered a relative contraindication for LPN. Overall, the ultimate decision to proceed with LPN should be based on the tumor characteristics and the surgeon's skill and experience with such an approach.

2.2 Preoperative preparation

Preoperative evaluation includes routine preoperative investigations as well as a computed tomography angiogram of the abdomen to delineate renal vasculature. Renal scintigraphy is obtained if there is a question about the global renal function. Preoperative medical clearance should be obtained when there is any question of the patient's fitness for major abdominal or vascular surgery. We routinely cross-match 4 units of packed red blood cells on demand. Mechanical bowel preparation of one bottle of magnesium citrate is given the evening before the surgery, and intravenous prophylactic antibiotics are given prior to entering the operating room.

2.3 Operative technique

A substantive LPN entails renal hilar control, transection of major intrarenal vessels, controlled entry into and repair of the collecting system, control of parenchymal blood vessels, and renal parenchymal reconstruction, all usually under the pressure of minimizing warm ischemia. As such, significant experience in the minimally invasive environment, including expertise with time-sensitive intracorporeal suturing, is essential. LPN can be approached either transperitoneally (our preferred approach) or retroperitoneally based on the surgeon's experience and the tumor location. The transperitoneal approach is usually chosen for anterior, anterolateral, lateral, and upper-pole apical tumors. Retroperitoneal

laparoscopy is reserved for posterior or posterolaterally located tumors. A retrospective, match-pair comparison of 105 patients who underwent either transperitoneal or retroperitoneal approaches for T1a renal masses demonstrated that both approaches provide comparable surgical and functional results [16]. Although studies report shorter operative time, decreased blood loss and shorter hospital stay with the retroperitoneal approach [16, 17], many centers prefer the transperitoneal approach for its greater working space and easy tumor accessibility [18].

After induction of general anesthesia, a Foley catheter and nasogastric tube are placed prior to patient positioning. Cystoscopy and ureteral catheter placement are performed if preoperative imaging indicates a risk of collecting system violation during resection of the lesion (a requirement for intraparenchymal resection greater than 1.5 cm or tumor abutting the collecting system). Although many laparoscopists prefer to place their patients at a 45 to 60° angle in the flank position, we prefer to place our patients undergoing renal surgery in the lateral flank position at 90°. This provides excellent access to the hilum and allows the bowel and spleen (on the left side) to fall off the renal hilum during procedures complicated by bowel distention.

Laparoscopic surgery is performed using a transperitoneal approach with a Veress needle, directly using the Optiview (Ethicon Endo-surgery ®) trocar system, or using the Hassan technique, to attain pneumoperitoneum. Three to four ports (including two 10-12 mm ports) are routinely placed in our technique. Exposure of the kidney and the hilar dissection are performed using a J-hook electrocautery suction probe or by using the ultrasound energy-based harmonic shears (Ethicon Endo-surgery ®). This is done by reflecting the mesocolon along the Line of Toldt, leaving Gerota's fascia intact. Mobilizing the kidney within this fascia, the ureter is retracted laterally, and cephalad dissection is carried out along the psoas muscle leading to the renal hilum. Once the tumour is localized, we dissect the Gerota's fascia and defat the kidney, leaving only the perinephric fat overlying tumor (Figure 8.1). Intraoperative ultrasonography with a Philips Entos LAP 9-5 linear array transducer (Philips ®) can be used to aid in tumor localization if it is not exophytic or if the tumor is deep into the renal parenchyma. A laparoscopic vascular clamp (Karl Storz ®) is placed around both the renal artery and the renal vein (without separation of the vessels) for hilar control in cases associated with central masses and heminephrectomy procedures, as described by Gill et al [19] (Figures 8.2-8.4).

Conversely, during a retroperitoneoscopic nephrectomy, the renal artery and vein are dissected separately to prepare for placement of bulldog clamps on the renal artery and vein individually. Mannitol may be used (0.5 g/kg intravenously) prior to hilar clamping or renal hypothermia. Resection of renal parenchyma is performed with cold scissors (Figures 8.5-8.10), and the specimen is retrieved using a 10-cm laparoscopic EndoCatch bag (US Surgical Corporation, Norwalk, Connecticut ®) and sent for frozen section analysis (sometimes with excisional biopsy from the base) to determine the resection margin status (Figures 8.17 and 8.18).

Hemostasis is accomplished using intracorporeal suturing, argon beam coagulator, and hemostatic matrix (FloSeal®, Baxter, Vienna, Austria) application in a manner previously described by others (Figures 8.10-8.16) [20-23].

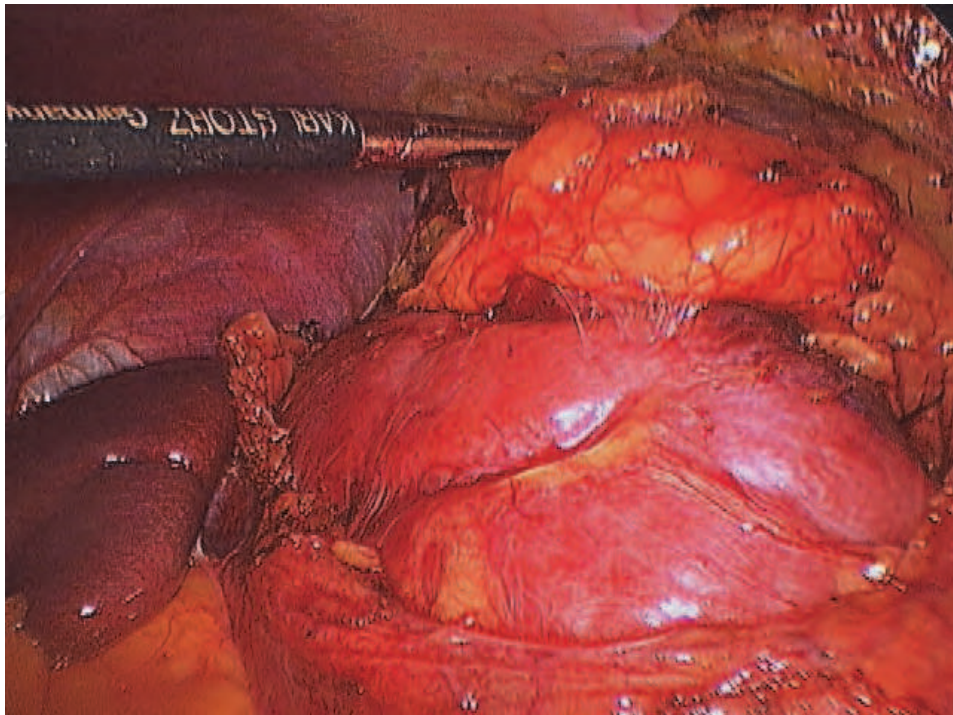


Fig. 8.1. Defatted kidney except area overlying the tumor

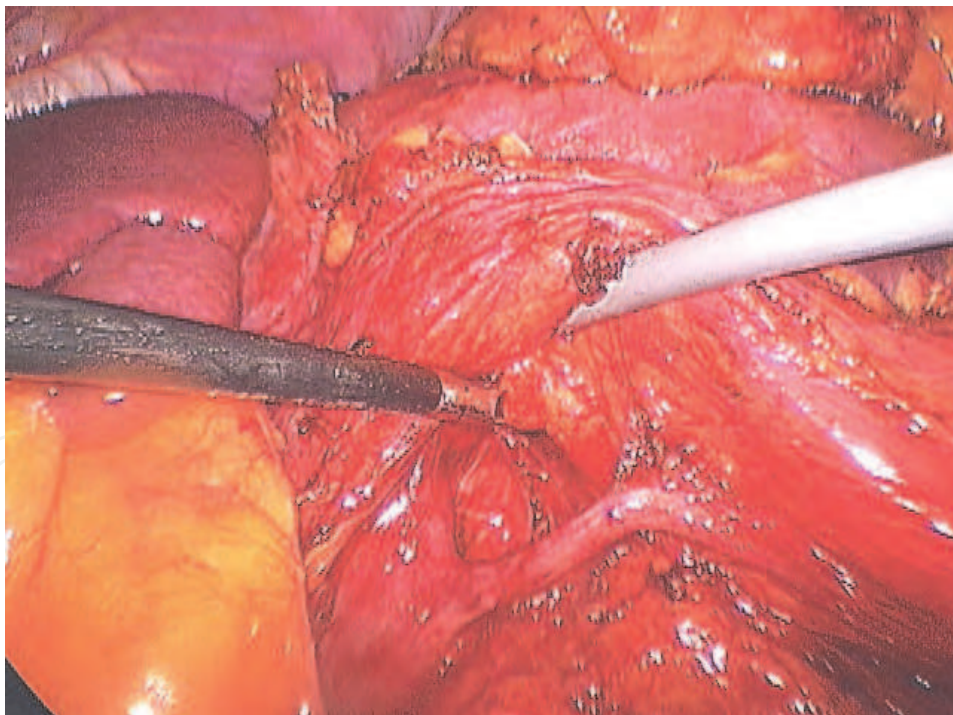


Fig. 8.2. Exposed renal hilum.

Intravenous injection of indigo carmine dye is used to delineate any collecting system violation, or retrograde injection of this dye via a ureteric catheter if it was inserted perioperatively. Any identifiable leak in the collecting system is oversewn with 4-0 absorbable sutures using the freehand intracorporeal laparoscopic technique.

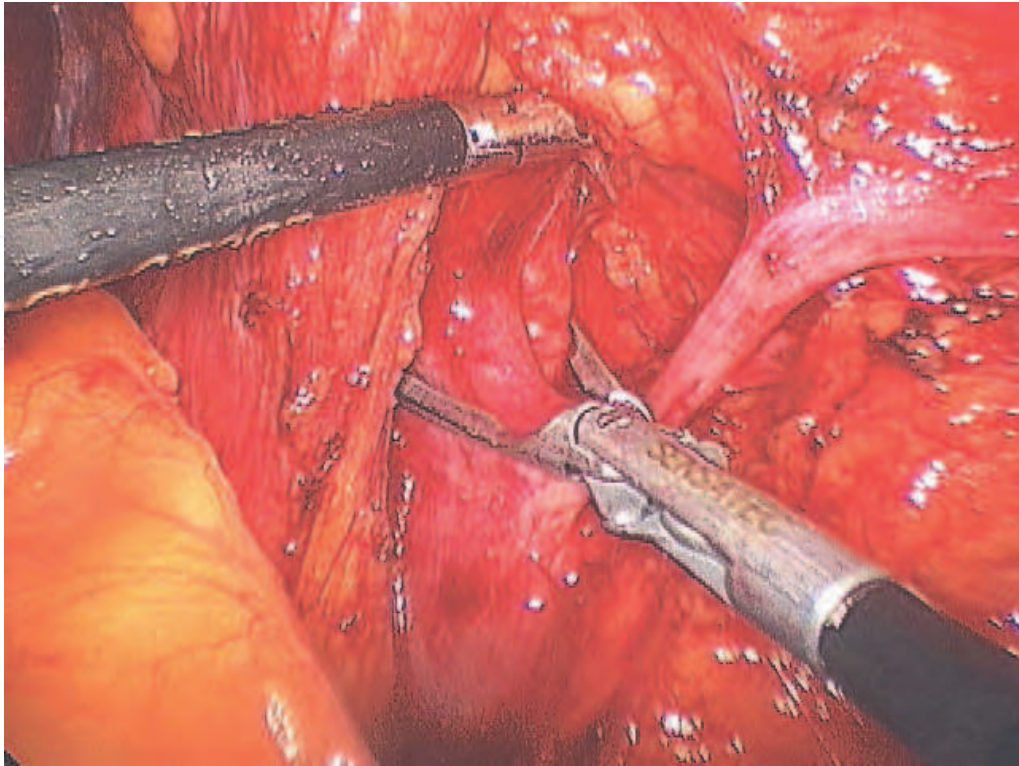


Fig. 8.3. Exposed hilum ready for clamping.

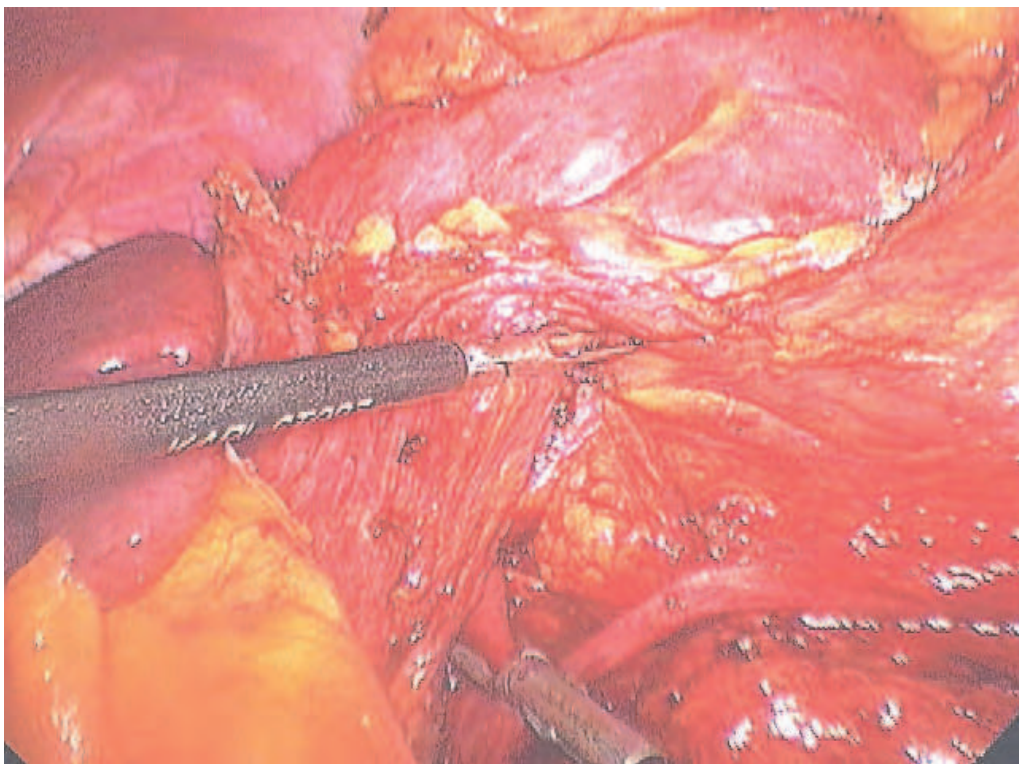


Fig. 8.4. Clamped renal hilum

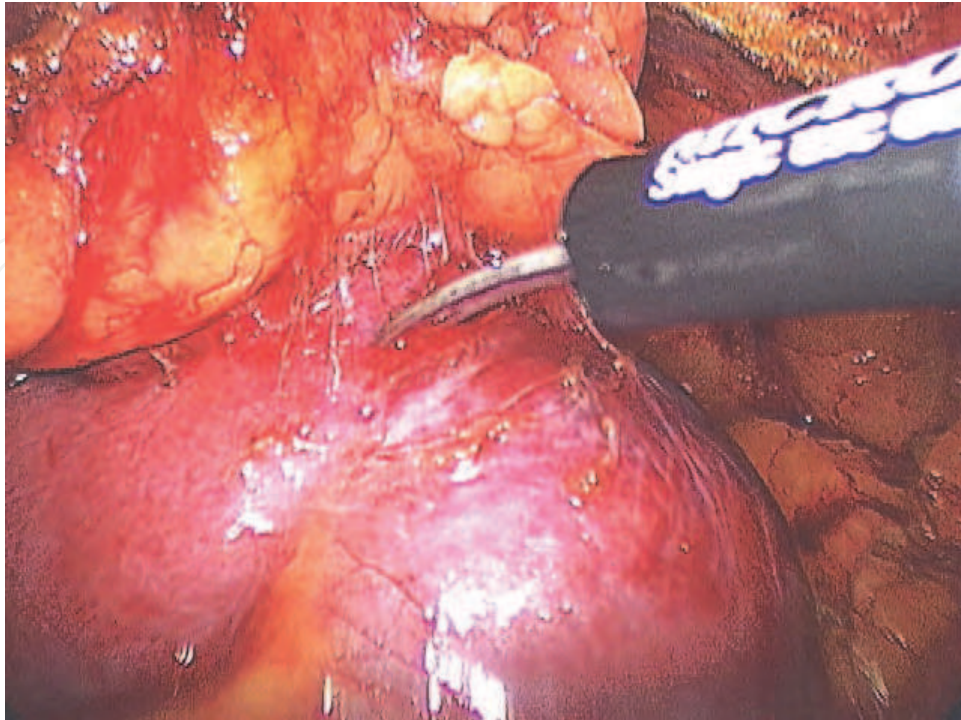


Fig. 8.5. Tumor resection using the cold scissor.

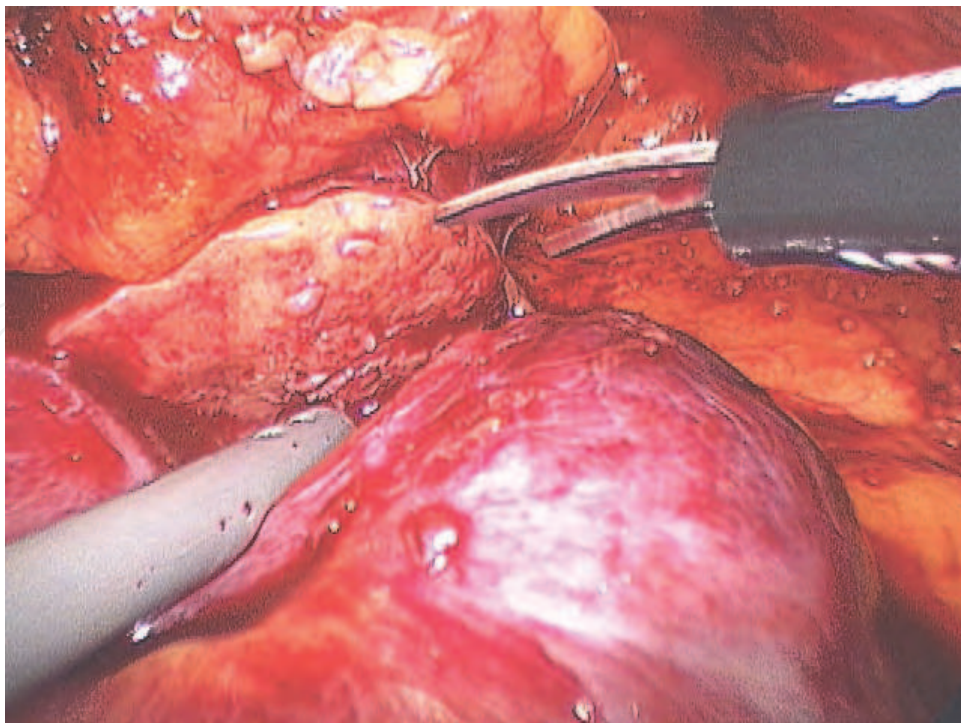


Fig. 8.6. continued tumor resection with surrounding normal parenchyma.

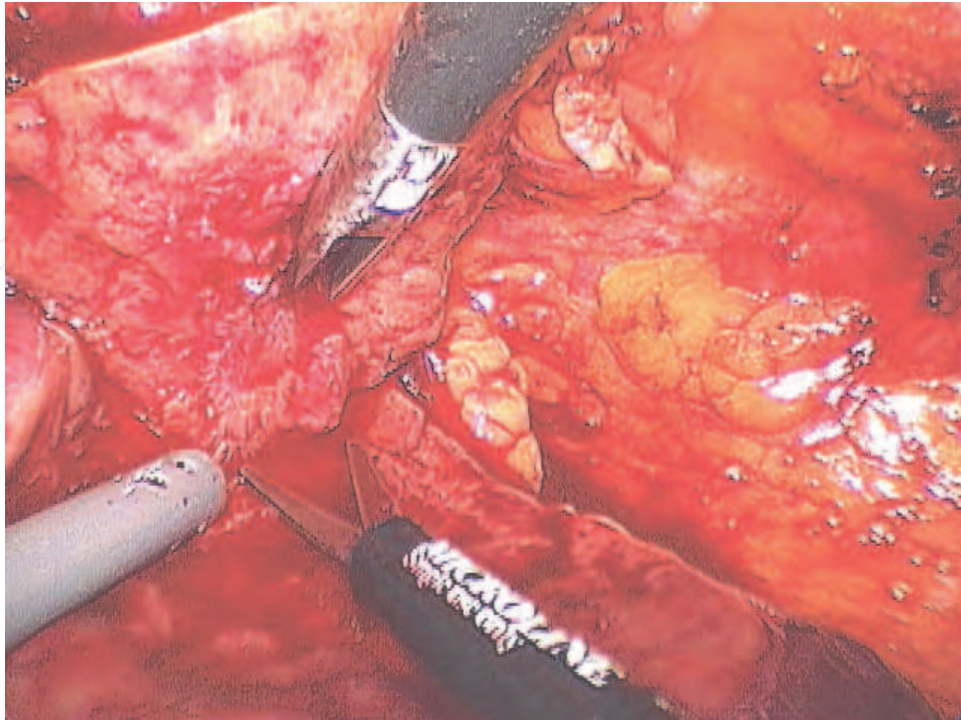


Fig. 8.7. Continued tumor resection.

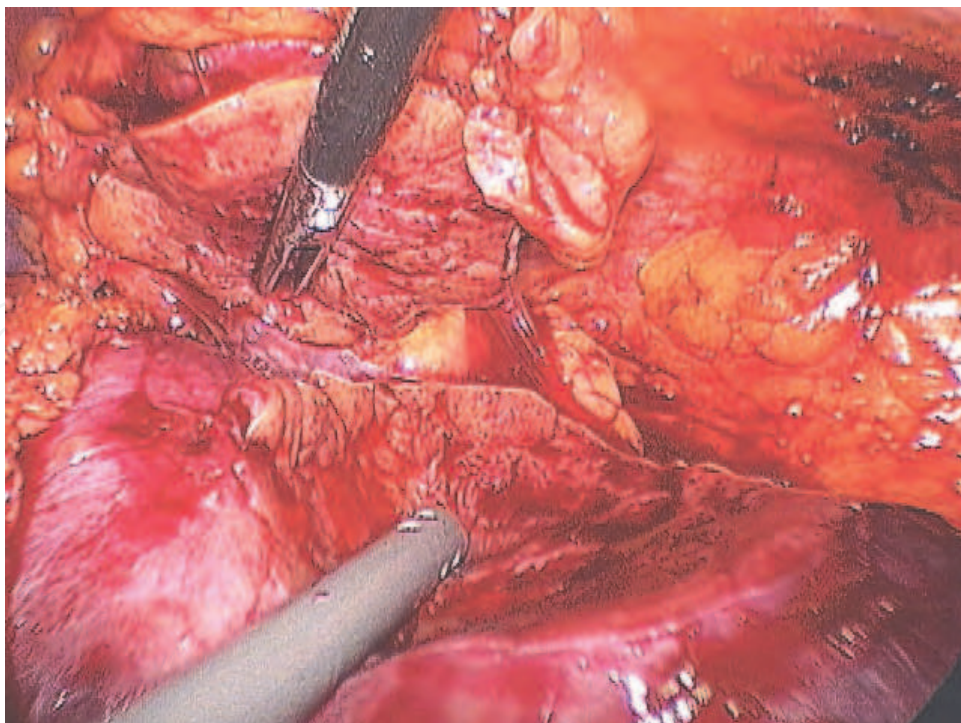


Fig. 8.8. Completely detached tumor.

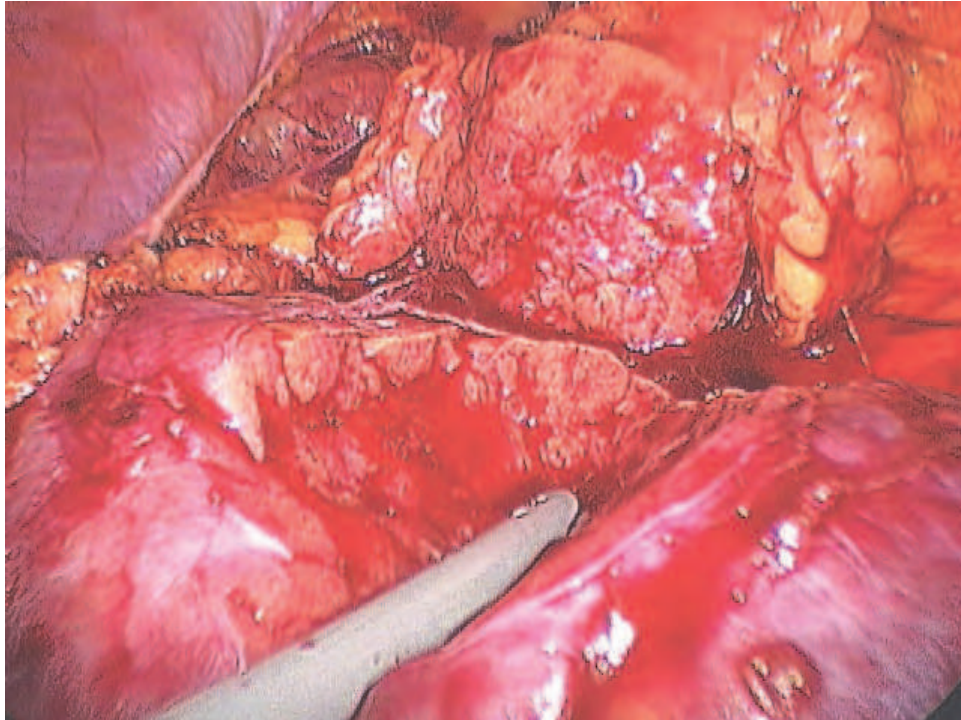


Fig. 8.9. Completely detached tumor with good surrounding parenchyma.

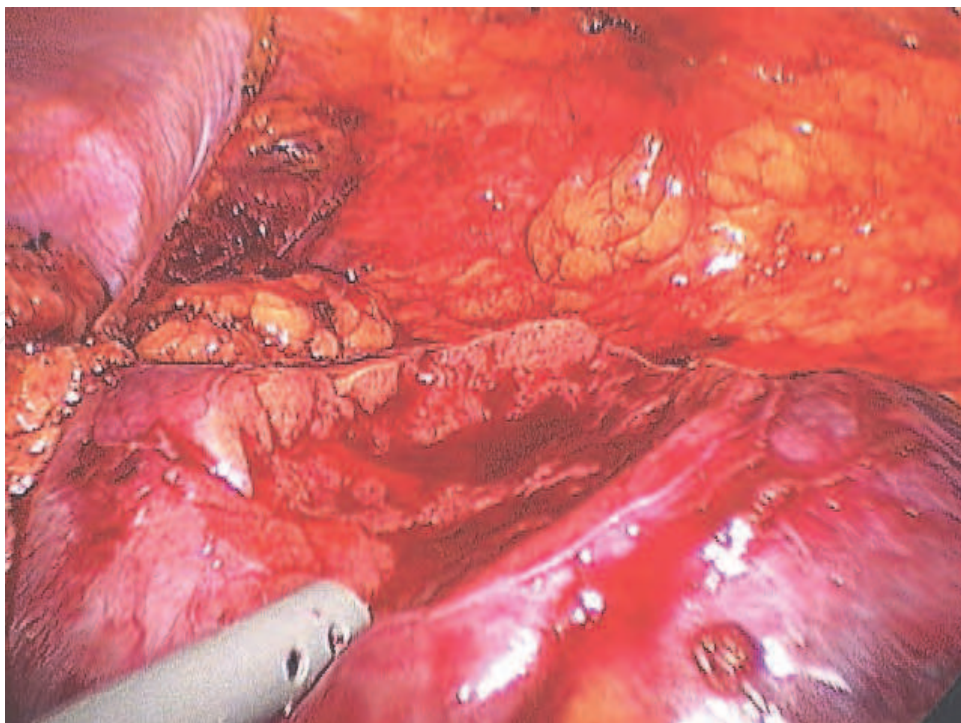


Fig. 8.10. Tumor bed.

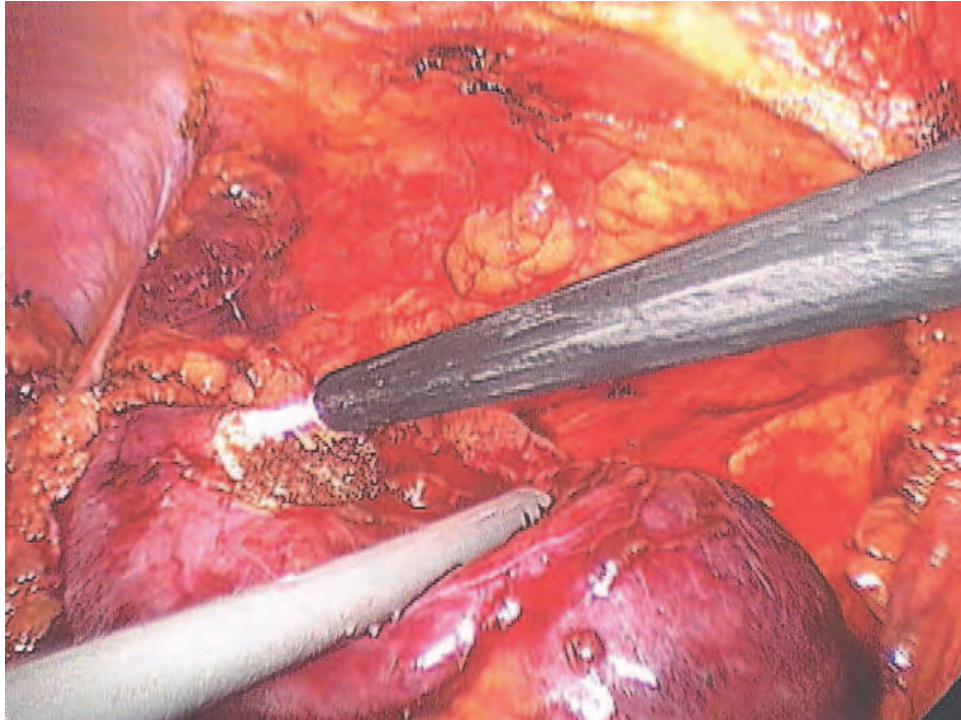


Fig. 8.11. Argon beam coagulator for bed hemostasis.

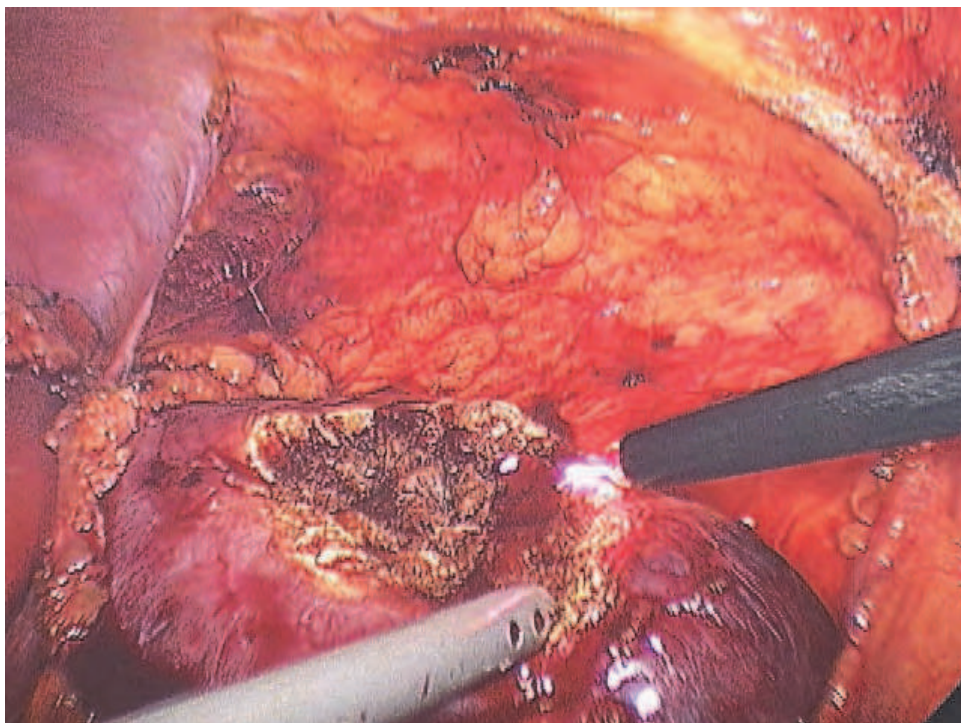


Fig. 8.12. Argon beam coagulator for bed hemostasis.

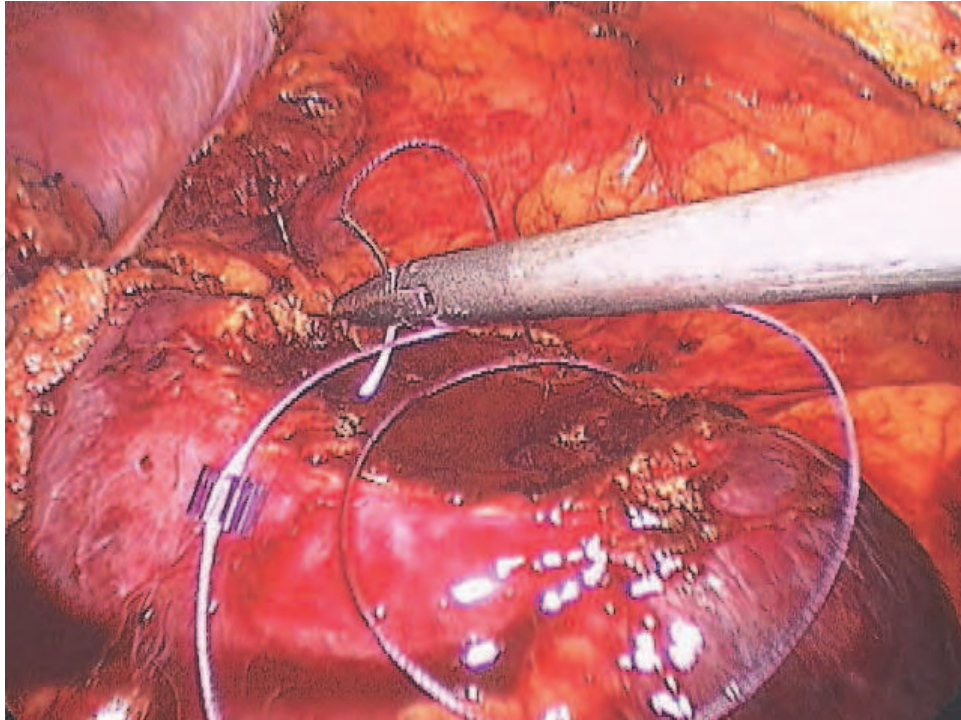


Fig. 8.13. Parenchymal intracorporeal suturing with Lapra-TY at one end.

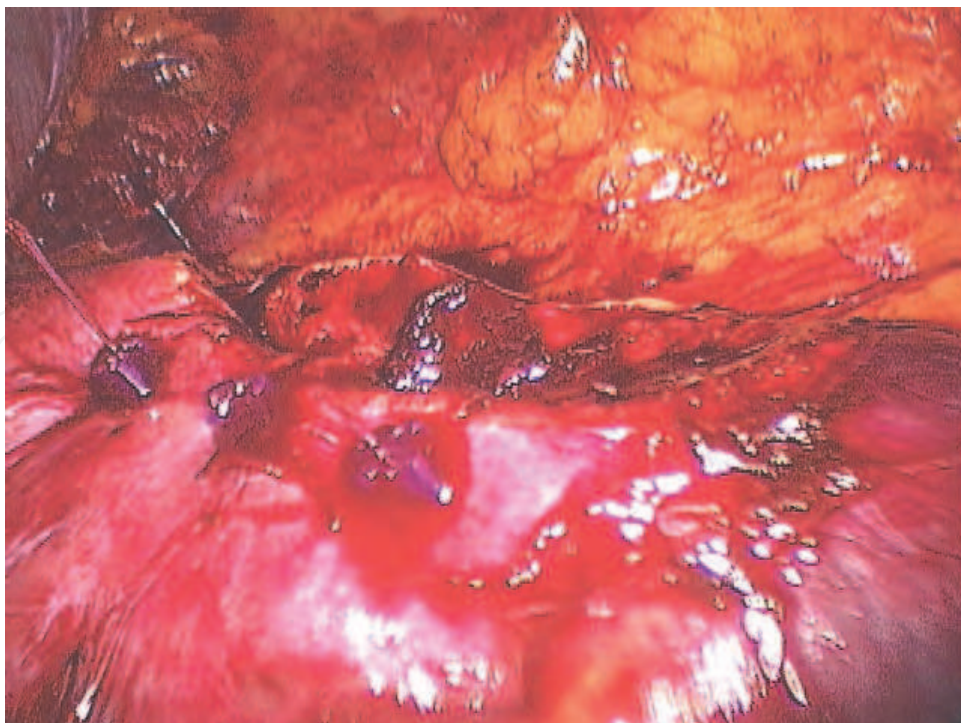


Fig. 8.14. Completed sutures with Lapra-TY on both ends.

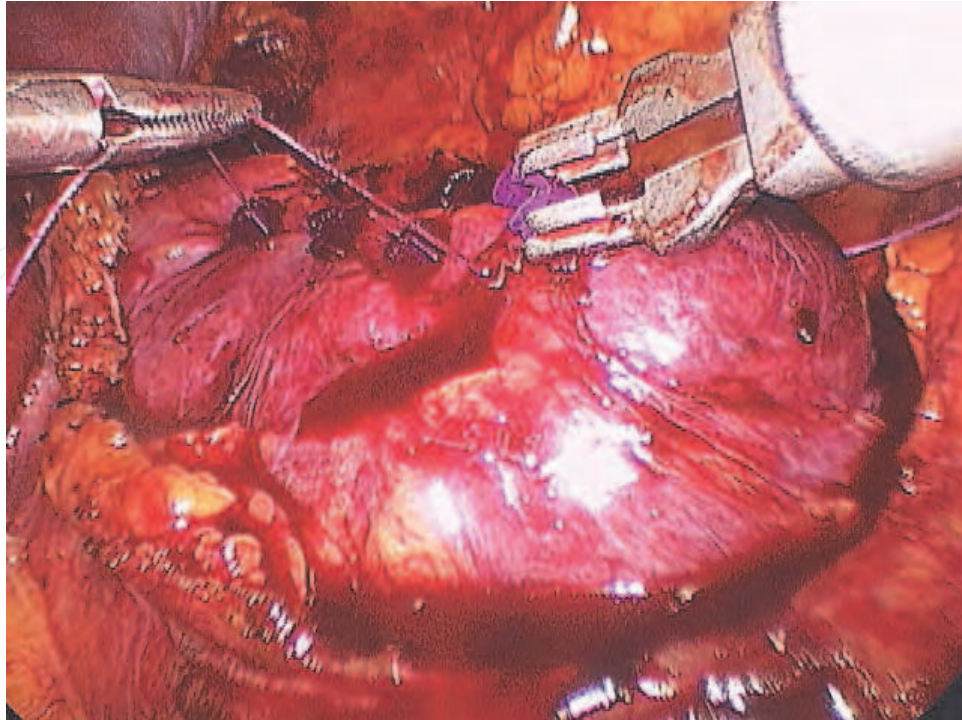


Fig. 8.15. Parenchymal suturing with Lapra-TY.

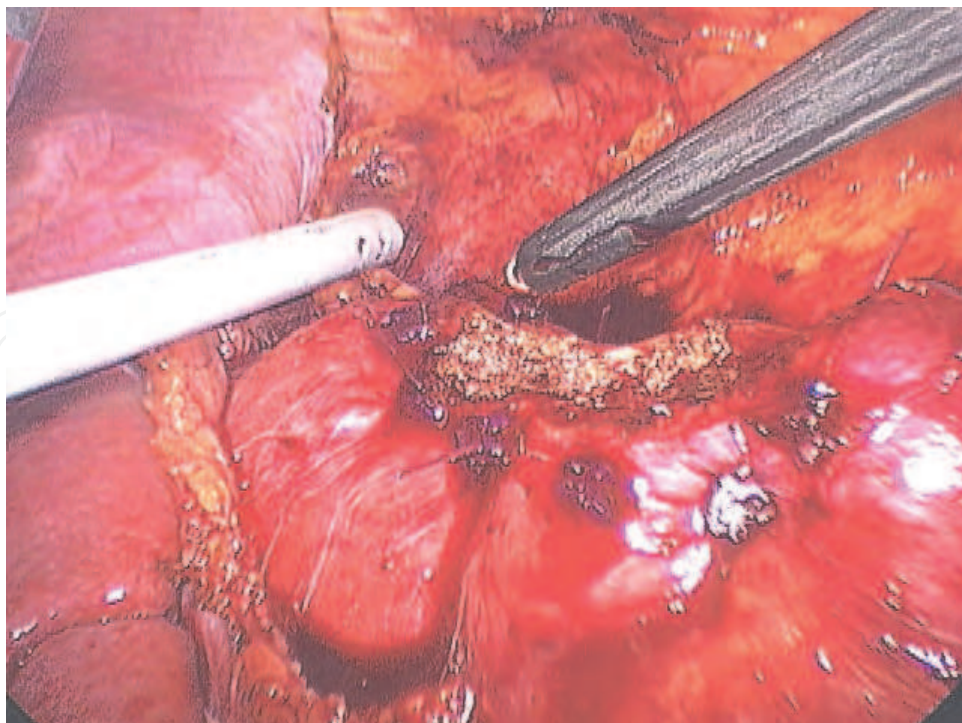


Fig. 8.16. Hemostasis with Argon beam coagulator after hilar unclamping.

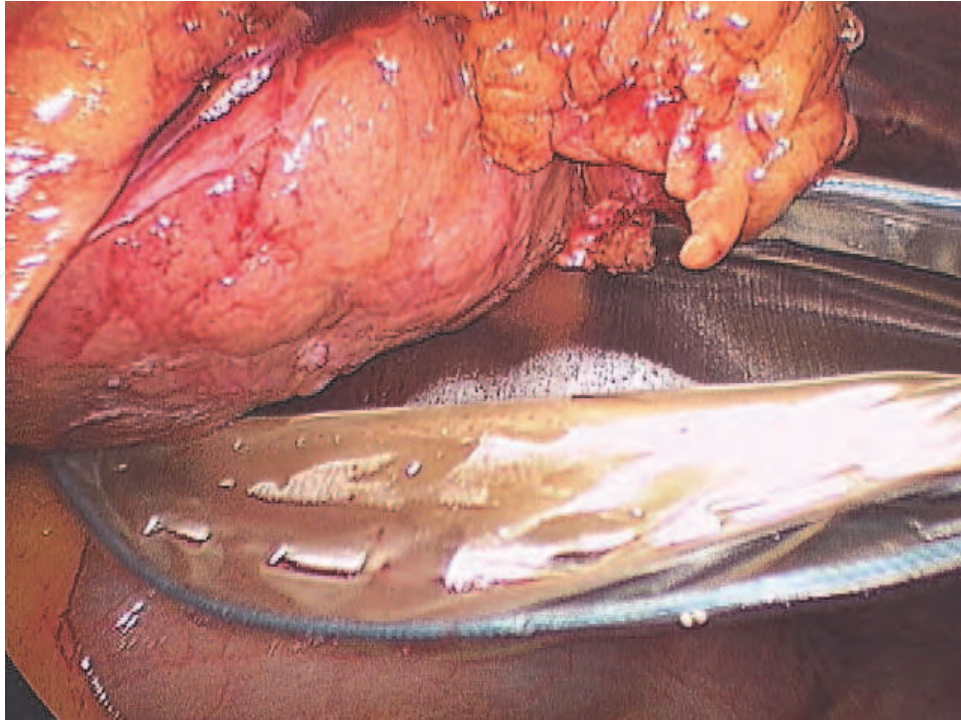


Fig. 8.17. Tumor entrapment in an Endocatch bag.

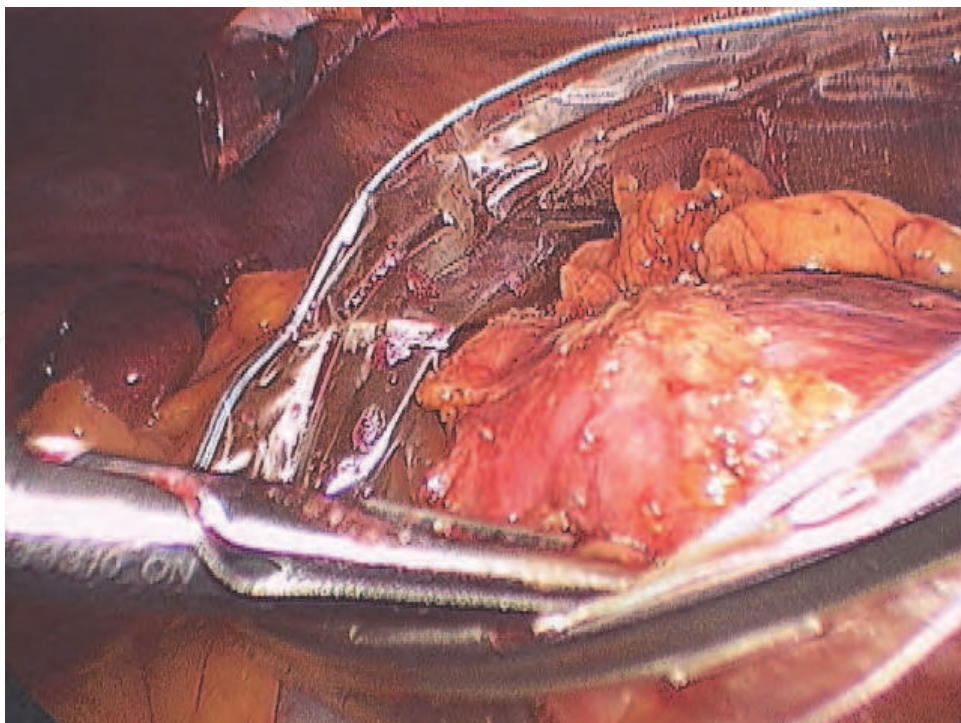


Fig. 8.18. Tumor completely entrapped.

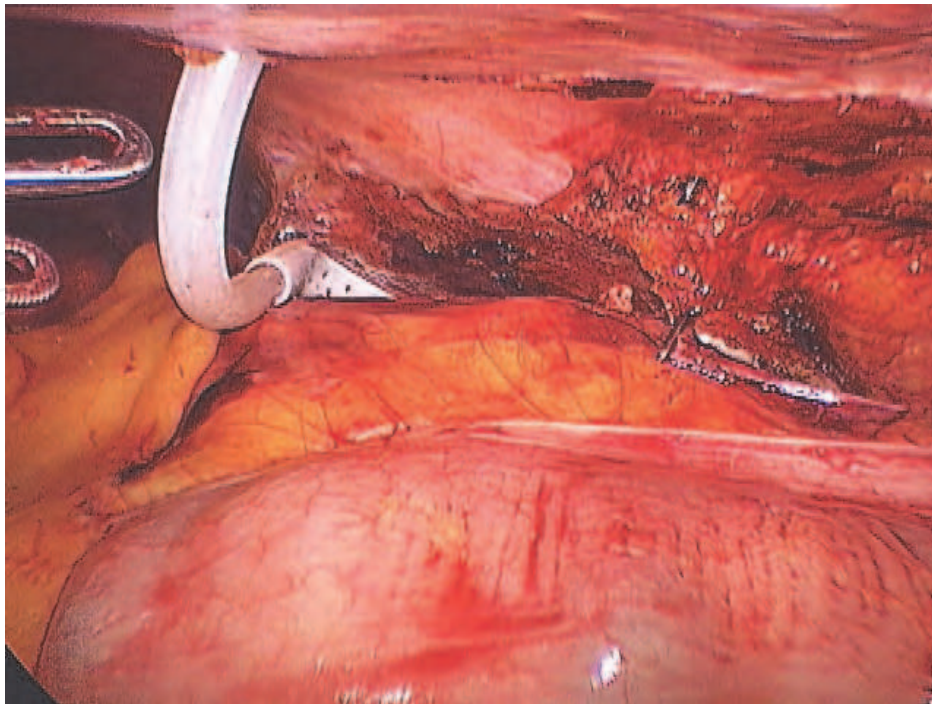


Fig. 8.19. Percutaneous drain around the operated site.

If the collecting system is entered, ureteral stenting additional to a Jackson-Pratt percutaneous drain placement is routinely performed (Figure 8.19). Specific figure-of-eight sutures are placed at the site of visible individual transected intrarenal vessels using a CT-1 needle and 2-0 Vicryl suture. Parenchymal closure is achieved by placing prefashioned rolled tubes or packets of oxidized cellulose sheets (Fibrillar®, Ethicon) into the parenchymal defect. Braided 2-0 absorbable sutures are used to bolster the sheets into position, and Floseal® is applied over the operative site using a laparoscopic applicator. We perform our parenchymal repair using multiple interrupted 2-0 absorbable sutures and securing them in position using absorbable polydioxanone polymer suture clips (Lapra-TY®, Ethicon, Endosurgery). Placing one Lapra-TY clip to the end of the suture then another one to the opposite side after compressing the kidney achieves this (Figures 8.13-8.15). Surgeons can also use Hem-o-Lok® in the place of Lapra-Ty® for parenchymal compression, or the combination of the two for a “sliding technique”.

This modification has resulted in a significant reduction of our warm ischemia time that was consumed primarily by intracorporeal suturing. Once renorrhaphy is completed, the vascular clamp is released, and the complete hemostasis and renal revascularization is confirmed. Whenever possible, the perinephric fat and Gerota's fascia is re-approximated. We extract the resected tumor along with its containing bag through a small extension of the lowermost abdominal port site incision. Laparoscopic exit under direct vision is performed once the 10-12 mm ports are closed.

3. Issues in laparoscopic partial nephrectomy

3.1 Warm ischemia and renal hypothermia

The highly differentiated cellular architecture of the kidney is dependent on the primarily aerobic renal metabolism. As such, the kidney is acutely vulnerable to the anaerobic insult

conferred by warm ischemia. The severity of renal injury and its reversibility are directly proportional to the period of warm ischemia time (WIT) imposed on the unprotected kidney. The optimal warm ischemia time remains controversial. Previous studies demonstrated that recovery of renal function is complete within minutes after 10 minutes of warm ischemia, within hours after 20 minutes, within 3 to 9 days after 30 minutes, usually within weeks after 60 minutes, and incomplete or absent after 120 minutes of warm ischemia [24-26]. A 5-year, multi-centre study of WIT in LPN vs. OPN cases (n=1800) reported that the mean WIT was 30.7 minutes and 20 minutes, respectively, in each group [27]. Though the incidence of pre-operative chronic kidney disease (CKD, defined as serum creatinine >2.0 mg/dl) was measured to be 1.6% and 6.4% in each respective group, the post-operative incidence of acute renal injury was 0.9% in both groups. Unfortunately, most classic studies of WIT used crude methods of determining renal function. More recent studies, including those that implement mercaptoacetyl triglycine (MAG3) lasix renal scintigraphy to more accurately assess kidney function, have resulted in more refined guidelines.

A series of 56 consecutive LPN cases performed by a single surgeon at a single institution, using pre-operative and post-operative MAG3-lasix renal scintigraphy, demonstrated a relationship between WIT (minutes) and renal differential function (RDF) [5]. Interestingly, the authors noted that the relationship between WIT and declining kidney function was more pronounced after 32 minutes. This suggests that within 30 minutes, focus should be on limiting resection margins, careful closure of the collecting system, and hemostasis.

Roles for cold ischemia and no ischemia have also been investigated. Also using renal scintigraphy analysis, Tatsugami and colleagues reported that, based on preoperative and postoperative analysis by renal scintigraphy of patients after OPN and LPN, cold ischemia conferred an advantage to postoperative recovery of affected renal function. The authors suggested that cold ischemia should be considered if the patient is at risk of renal function deterioration, or when warm ischemia time is expected to be >30 minutes [28]. A retrospective comparison of warm ischemia versus no ischemia during partial nephrectomy on a solitary kidney in OPN and LPN cases showed that patients with warm ischemia (median of 21 min) were more likely to develop acute renal failure (O.R. 2.1, p=0.04) and post-op GFR <15 ml/min/1.73 m² (OR 4.2, p=0.007) [29]. However, a surgeon selection bias was present. Patients who received warm ischemia also had significantly higher pre-op GFR and larger tumors. Even so, the authors concluded that PN without any ischemia could be considered when technically feasible.

In 2009, an expert international panel recommended that WIT be kept to <20 minutes, and that in difficult cases, cold ischemia be started immediately and should not exceed 35 minutes [30]. Currently, the debate about the appropriate and safe amount of WIT in partial nephrectomy remains unresolved. Though 30 minutes remains the acceptable limit in practice, further studies involving sophisticated means of assessing renal function may prompt changes in the future.

3.2 Hilar clamping

In LPN, clear visualization of the tumor bed is imperative. Hilar clamping achieves a bloodless operative field and decreases renal turgor. Hence, hilar clamping enhances the

achievement of a precise margin of healthy parenchyma during tumor excision, suture control of transected intrarenal blood vessels, precise identification of calyceal entry followed by water-tight suture repair, and renal parenchymal reconstruction. The controlled surgical environment provided by transient hilar clamping is advantageous for a technically superior LPN. The small completely exophytic tumor with minimal parenchymal invasion may be wedge resected without hilar clamping as it would have been performed in open surgery [31, 32].

However, recent studies have demonstrated favorable results in LPN procedures conducted without hilar clamping, or by clamping only the renal artery or one of its segmental branches. Theoretically, the technique of hilar unclamping can create a less clear operative field, resulting in uncontrolled bleeding, unidentified injuries to the collecting system, and difficulty identifying the correct excisional plane. The necessity of hilar or arterial clamping becomes clear in cases where tumor resection is difficult or complex, such as tumors that are partially exophytic with a certain depth of parenchymal invasion or are large in size. A recent retrospective case series of patients who underwent LPN with or without renal artery clamping—deemed necessary when the depth of tumor invasion was greater than 50% of the renal parenchyma as seen via CT or MRI—showed that although mean operative time was longer in the clamped group ($p=0.007$), there were no significant differences in peri-operative or post-operative complications [33]. Groups were not evenly balanced, with the rate of malignant tumors confirmed via pathology being 18% in the non-clamped group, and 90% in the clamped group ($p=0.002$), suggesting. Many investigators have advocated clamping of the renal artery alone (rather than the whole pedicle. This technique facilitates precise excision, repair in a bloodless field, and continuous venous drainage to decrease venous oozing and reduce possible free-radical damage during ischemic periods. Gerber and Stockton conducted a survey to assess the trend among urologists in PN practice and found 41% of the respondents clamp the renal artery only to obtain vascular control [34]. Clamping of a segmental artery alone has also been investigated. A retrospective study at one centre has demonstrated that clamping of a single segmental artery in patients undergoing LPN for T1a or T1b tumors resulted in increased blood loss ($p<0.006$) and WI time ($p<0.001$), but equivalent post-operative complication rates, and better post-operative renal function at 3 months ($p<0.001$) compared to renal artery clamping [35]. It was noted, however, that the size ($<3.5\text{cm}$) and location (polar or posterior) of the tumor influenced the decision to attempt segmental artery clamping, suggesting that the novel technique was safe and feasible in select patients. Ultimately, clamping results in renal ischemia, and thus necessitates precise and expedient tumor excision and renal reconstruction. Although newer methods have been shown to be feasible, these should be reserved for select patients in the care of an experienced surgeon comfortable with these techniques.

4. Hemostasis

One of the essential elements in PN is to achieve secure renal parenchymal hemostasis. The classic technique for achieving hemostasis of the parenchymal vessels that are transected during LPN is precise suture ligation followed by a tight reapproximation of the renal parenchyma (renorrhaphy) over absorbable bolsters [36]. The renal hilum or the renal artery is cross-clamped to halt renal blood flow, similar to open PN. In efforts to decrease blood loss and warm ischemia, many hemostatic devices and materials have been reported. These

are frequently used in combination and differ in their indication, efficacy, side-effects, equipment requirements and cost [34].

4.1 Hemostatic techniques

4.1.1 Parenchymal compression

Several techniques for achieving hemostasis by parenchymal compression have been described. These techniques are intended for achieving hemostasis in the resection of polar tumors. Circumferential compression of the kidney proximal to the tumor decreases blood flow to the resection site without requiring clamping.

Several recent human reports suggest that a clamping of the renal parenchyma without hilar clamping is feasible for hemostasis during LPN and open PN [37-41]. A clamp may be used on the parenchyma without dissection of the renal hilum. Clamping is limited to polar tumors and positioning the clamp can sometimes be challenging. Additionally, there are risks that the clamp may slip, causing hemorrhage, or that the pressure of the clamp may cause damage to the underlying parenchyma. Verhoest et al [42] report the use of a Satinsky clamp (Xomed Micro, France) in 5 patients undergoing LPN. The mean tumor diameter was 3.06 cm and all were polar. Mean operative time was 238 minutes and mean blood loss was 250 mL with no transfusions or other complications. Other authors have reported similar feasibility with a laparoscopic Nussbaum clamp (Aesculap AG, Tuttlingen, Germany ®) [43] and their own proprietary circumferential clamp [44].

Other methods of parenchymal compression have also been described. The double loop tourniquet technique consists of two U-loop strips of umbilical tape extending from a 17 Fr plastic sheath described by Gill et al [45] in a single LPN. McDougall et al [2] and Cadeddu et al [46] have reported the use of a plastic cable tie for LPN in a pig model [2]. Compression with pledgeted sutures [47] and an Endoloop [48] have also been reported in pigs.

4.1.2 Argon beam coagulator

The argon beam coagulator (ABC) (CONMED, Utica, NY ®) is used for hemostasis along the surface of retained renal parenchyma in LPN. It is not used to coagulate larger blood vessels or for dissection. ABC works by conducting electrical current to tissue along a jet of inert, non-flammable argon gas. This gas blows away blood and other liquids on the tissue surface, enhancing visualization of the bleeding site as well as eliminating electric current dissipation in the blood. Smoke is also reduced as argon gas displaces oxygen. The surgeon should be aware of argon gas flow rates and pneumoperitoneum pressures in efforts to prevent tension pneumothorax[49] and gas embolism [50, 51]

Hernandez et al [52] have reported the successful use of the ABC for hemostasis in 25 canine partial nephrectomies without hilar clamping. The mean blood loss was 135 cc and mean depth of tissue necrosis was 2.4 mm. Meanwhile, Lucioni et al [53] have studied the use of the ABC as the sole hemostatic agent during 24 porcine laparoscopic heminephrectomies with hilar clamping. A higher power setting and completion nephrectomy were each required in one case to control bleeding.

Although no human trials reporting the efficacy of ABC have been reported, its use in conjunction with other methods is frequent [34].

4.1.3 Ultrasonic shears

Ultrasonic shears, also known as the *harmonic scalpel* (*Ultracision* or *Harmonic ACE*, Ethicon Endo-Surgery, Cincinnati, OH ®), allow for simultaneous tissue division and hemostasis. Hemostasis is achieved by a titanium blade vibrating at 55 000 Hz which achieves thermal denaturation of tissue into a coagulum. Animal and human studies by Jackman et al [54] and Tomita et al [55] respectively suggest that ultrasonic shears alone are insufficient for hemostasis of arcuate or larger vessels.

Harmon et al [32] evaluated its use in 15 patients undergoing LPN with small tumors (mean size 2.3 cm) without vascular clamping, and reported a mean blood loss of 368 ml and a mean operative time of 170 minutes. These investigators also employed an argon beam coagulator and oxidized cellulose gauze. Guillonnet et al [56] performed a nonrandomized retrospective comparison of two techniques for LPN, that is without and with clamping the renal vessels. In group 1 (12 patients) PN was performed with ultrasonic shears and bipolar cautery without clamping the renal vessels; while in group 2 (16 patients) the renal pedicle was clamped before tumor excision with a cold knife and hemostasis achieved by sutures and hemostatic mesh. All tumors but 1 were exophytic. Mean renal ischemia time was 27.3 minutes (range 15-47 minutes) in group 2 patients. Mean laparoscopic operating time was 179.1 minutes (range 90-390 minutes) in group 1 compared with 121.5 minutes (range 60-210 minutes) in group 2 ($p = 0.004$). Mean intraoperative blood loss was significantly higher in group 1 than in group 2 (708.3 versus 270.3 ml, $p = 0.014$). Surgical margins were negative in all specimens.

Ultrasonic shears are primarily useful in small peripheral lesions which may be excised without vascular occlusion. Disadvantages of ultrasonic shears used for this purpose include tissue charring, tissue adherence, and an inexact line of parenchymal incision with poor visualization of the tumor bed. They are also inadequate as a sole hemostatic agent and not recommended for larger or deeper tumors. The *harmonic scalpel* is not recommended when vascular clamping is employed as the harmonic scalpel is slower than other methods and may result in kidney damage secondary to increased warm ischemic time [56].

4.1.4 Water (hydro) jet dissection

Hydro-jet (Erbe Elektromedizina GmbH, Tübingen, Germany ®) involves using a high-pressure jet of saline to selectively dissect parenchymal tissue. Blood vessels and the collecting system are not penetrated if a 400-600 psi pressure is used [57]. Shekariz et al have investigated this technology during LPN with hilar control in the porcine model [58] and reported a virtually bloodless field with the vessels and collecting system preserved. Moizadeh et al [57] similarly evaluated hydro-jet assisted LPN in the calf model. Vessels were controlled with a BIClamp (Erbe Elektromedizina GmbH, Tübingen, Germany) bipolar instrument. Of 20 LPN, 18 were performed without hilar clamping and in 15 only the bipolar instrument was required for hemostasis. The mean Hydro-jet PN time was 63 minutes (range 13-150 minutes) and mean estimated blood loss was 174 ml (range 20 to 750 mL). Corvin et al [59] have also demonstrated the feasibility of Hydro-jet in wedge resection in the pig model.

The use of Hydro-jet dissection in LPN in humans has not been formally reported. Basting et al.[60] report the use of Hydro-jet in a series of 24 renal sparing surgeries performed for benign and neoplastic disease. Dissection took between 14 and 35 minutes and the average blood loss was 60mL with no significant complications. Shekarritz[61] describes unpublished data that hydro-dissection was successfully used in 6 open partial nephrectomies for RCC without hilar control. Dissection time was 20-30 minutes, blood loss ranged from 150-500 mL (mean 265 mL) and there were no complications.

4.1.5 Microwave coagulation

Microwave tissue coagulation (MTC) with the Microtaze device (Azwell, Osaka, Japan) utilizes a needle-type monopolar electrode which is inserted into the kidney repeatedly prior to renal incision. 2450 MHz of microwave energy is applied to tissue surrounding the electrode forming a conical-shaped wedge of coagulated tissue extending up to 10mm. Partial nephrectomy is then performed in the plane of coagulated tissue resulting in a relatively blood-free field. MTC necessitates mobilization of the entire kidney for appropriate probe insertion and has the potential for serious complications, as subsequently described.

Terai et al [62] have used MTC to perform LPN in 18 patients with peripheral tumors. They report a mean operative time of 240 minutes (range 131-390 minutes). Minimal blood loss occurred in 14 patients and 100-400mL blood loss occurred in the remaining. Postoperative complications which were managed conservatively included a hematoma in an anticoagulated patient and a 14-day urinary leak. A renal arteriovenous fistula that required embolization occurred in one patient. Finally, pelvicalyceal stenosis resulting in a nonfunctional kidney occurred in another patient. Similar complications have also been reported in OPN [63, 64]. Yoshimura et al [65], Satoh et al [66] and Itoh et al [67] have reported smaller MTC LPN series without such complications.

4.1.6 Radiofrequency ablation

Radiofrequency ablation (RFA) involves the delivery of energy via a needle causing coagulation around the inserted probe. Investigators have successfully used interstitial ablative technologies (like radiofrequency ablation and cryotherapy) as definitive in situ management of select renal lesions. Ablated tumors are left in situ, necessitating concerns about the oncologic effectiveness of ablation in the target lesion and the cost of radiographic follow-up. In RFA-assisted LPN, radiofrequency coagulation can be used prior to partial nephrectomy to achieve energy-based tissue destruction followed by resection of the ablated tissue. Resection of ablated tissue is relatively bloodless obviating the need for hilar clamping.

Wu et al [68] have recently published a series comparing 36 patients undergoing LPN with hilar clamping to 42 patients undergoing RFA-assisted robotic clampless partial nephrectomy. Tumors were larger in the RFA group (2.8 vs. 2.0cm), more often endophytic (52.6% vs. 16.1%) and collecting system reconstruction occurred more often (78.6% vs. 30.6%). Although operative time was longer in the RFA group (373 vs. 250 minutes), blood loss, transfusion rates, renal function and complication rates did not differ between groups. Zeltser et al [69] have also published a series of 32 tumors treated with RFA-assisted LPN.

Mean blood loss was 80 mL and there were no recurrences at a mean follow-up of 31 months. Other authors have also published series on this technique [70-72].

4.1.7 TissueLink

Another option that may be used for dissection and hemostasis is the TissueLink Floating Ball (TissueLink Medical, Inc., Dover, NH). This is a monopolar device that employs radiofrequency current for dissection and uses saline as a cooling medium. A total of 34 patients in several series were identified by us [73-76] which all had appropriate operative time, oncologic control, complications and blood loss when compared to other hemostatic devices.

4.2 Hemostatic materials

Hemostatic materials involve the application of a substance to the resection bed to effect hemostasis. Classes of hemostatic materials include fibrin sealants, gelatin matrix sealants, hydrogel based sealants and oxidized cellulose. The use of multiple hemostatic materials is routine in centers performing LPN [77].

These materials differ in their mechanism, cost, application conditions, uses, and tissue reaction. A rigorous comparison of these materials is beyond the scope of this chapter due to the number of products and absence of appropriate comparative studies. Concerns that arise when using these products include cost, risk allergic reaction, potential transmission of prion and other infectious diseases, and the need to mix two components and/or sequentially apply them.

Fibrin products include Tisseel (Baxter), Beriplast (CSL Behring GmbH), Hemaseel (HMN), Costasis (Cohesion Technologies), Vivostat (Vivostat A/S), and Evicel (Ethicon, Johnson & Johnson). Fibrin products must be applied to a dry surface and may offer both hemostasis and sealing of the collecting system [78]. Generally, these products include a concentrated solution of human fibrinogen which is mixed with thrombin and calcium chloride. The addition of aprotinin helps to slow the natural fibrinolysis occurring at the resection site. Natural bioabsorption eventually occurs from plasma-mediated lysis [79]. Fibrin sealants may also come in sprays [80]. Autologous fibrin sealants, such as Vivostat, have been developed in attempts to minimize this risk of infectious and allergic complications. Authors have demonstrated that fibrin sealants may be effective as the sole hemostatic technique or used in conjunction with other methods [79, 81, 82].

Gelatin matrix products provide thrombin, calcium, and bovine-derived gelatin granules. These agents include FloSeal (Baxter), which is our preferred hemostatic flowable agent to use during LPN. FloSeal may be applied to a wet surface and function only in parenchymal hemostasis. Unlike fibrin sealants, thrombin in these products converts fibrinogen from the patient's blood into a fibrin clot. The gelatin granules swell on contact with blood, creating a composite hemostatic plug with physical bulk that mechanically controls hemorrhage [83]. Gill et al [83] have reported a series of 131 patients, in which they compared their conventional technique of sutured renorrhaphy over a Surgicel bolster to the same technique with the addition of FloSeal. FloSeal significantly reduced overall complications (37% vs. 16%) and had a trend towards lower rates of hemorrhagic complications (12% vs. 3%). Wille et al [84], Richter et al [85] and Bak et al [86] have also described positive series.

Bovine serum albumin and glutaraldehyde tissue adhesive (BioGlue, Cryolife, Kennesaw, GA) is another sealant that is applied to a dry surface and controls both the renal parenchyma and collecting system. Glutaraldehyde exposure causes the lysine molecules of the bovine serum albumin, extracellular matrix proteins, and cell surfaces to bind to each other, creating a strong covalent bond. The reaction is spontaneous without needing the patient's coagulation factors. The glue begins to polymerize within 20 to 30 seconds and reaches maximal strength in approximately 2 minutes, resulting in a strong implant. The degradation process takes approximately 2 years, and it is then replaced with fibrotic granulation tissue. Several series support the use of BioGlue [87, 88].

Oxidized cellulose products include Surgicel (Johnson & Johnson, Somerville, NJ), Gelfoam (Pfizer, Inc., New York, NY) and Surgifoam (Johnson & Johnson). These products have hemostatic properties and can also be left as a bolster within the kidney to tamponade bleeding. Authors report the use of the bulk of these products to close fill parenchymal defects [89] although it is associated with a foreign-body reaction [90].

While numerous other hemostatic agents exist, these products represent the most frequently used materials. Newer products are currently being developed using various in vivo and in vitro models [91-93].

5. Morbidity

LPN improves upon the morbidity of open PN. Investigators from Cleveland Clinic analyzed the complications of their initial 200 cases treated with LPN for a suspected renal tumor [94] and reported that 66 (33%) patients had a complication: 36 (18%) patients had urologic complications, the majority of which was bleeding, and 30 (15%) patients had non-urologic complications. This experienced team also reported a decreased complication rate (16%) since they began using a biologic hemostatic agent as an adjunctive measure. Gill et al [19] compared 100 patients who underwent LPN with 100 patients who underwent OPN. The median surgical time was 3 hours vs 3.9 hours ($p < 0.001$), estimated blood loss was 125 ml vs 250 ml ($p < 0.001$), and mean WIT was 28 minutes vs 18 minutes ($p < 0.001$). The laparoscopic group required less postoperative analgesia, a shorter hospital stay, and a shorter convalescence. Intraoperative complications were higher in the laparoscopic group (5% vs 0%; $p = 0.02$), and postoperative complications were similar (9% vs 14%; $p = 0.27$). Functional outcomes were similar in the two groups: median preoperative serum creatinine (1.0 vs 1.0 mg/dl, $p < 0.52$) and postoperative serum creatinine (1.1 vs 1.2 mg/dl, $p < 0.65$).

Similarly, Beasley et al [95] retrospectively compared the result of laparoscopic PN to OPN using a tumor size-matched cohort of patients. Although the mean operative time was longer in the laparoscopic group (210 ± 76 minutes versus 144 ± 24 minutes; $p < 0.001$), the blood loss was comparable between the two groups (250 ± 250 ml vs 334 ± 343 ml; $p =$ not statistically significant). No blood transfusions were performed in either group. The hospital stay was significantly reduced after LPN compared with the open group (2.9 ± 1.5 days vs 6.4 ± 1.8 days; $p < 0.0002$), and the postoperative parenteral narcotic requirements were lower in the LPN group (mean morphine equivalent 43 ± 62 mg vs 187 ± 71 mg; $p < 0.02$).

These initial results have been reproduced in recent studies. In an analysis of 1800 OPN and LPN cases for single renal T1 tumours, LPN was associated with shorter operative time,

decreased operative blood loss, and shorter hospital stay ($p < 0.01$) [27]. Another multicentre study of 10 years' worth of data demonstrated decreased transfusion incidence and estimated blood loss less (293 vs 418 cc) in LPN compared to OPN [96].

Interestingly, published studies have not demonstrated increased morbidity for LPN for T1b tumors. A retrospective study at a single centre compared operative and post-operative complications in patients who underwent LPN for tumors > 4 cm to those who underwent LPN for tumors ≤ 4 cm. The authors concluded that there were no significant differences observed with respect to operating time, transfusion requirements, post-operative complications, or hospital stay, suggesting that LPN, from a morbidity standpoint, is feasible for tumors > 4 cm in carefully selected patients [97].

Despite the absence of a prospective randomized controlled trials, these congruent series suggest improved morbidity from LPN relative to open PN.

6. Oncologic results

Longitudinal studies for LPN for tumors ≤ 4 cm and > 4 cm have demonstrated the efficacy and safety of this approach comparable to OPN and other laparoscopic techniques. The 3 year cancer-specific survival for patients with a single cT1N0M0 RCC has been reported similar for OPN and LPN (99.3% LPN and 99.2% OPN) [27]. In a 5 year, intermediate-term study, comparing laparoscopic radical nephrectomy (LRN) and LPN ($n=35$) for T1b-T3N0M0 RCC, overall mortality (11% in each group), cancer-specific mortality (3% in each group) and recurrence (3% vs 6%) rates ($p=0.4$) were equivalent [9]. Recurrence-free survival in each group was 96%. The longest follow-up study to date is a retrospective 7-year follow-up study comparing oncologic outcomes of LPN and OPN for a single cT1 cortical tumor 7cm or less. Metastases free survival with a minimum of 7 years follow-up was equivalent in both groups (97.5% LPN vs. 97.3% OPN, $p=0.47$.) After multivariable analysis that accounted for the propensity to undergo LPN, surgical approach was not associated with a significant difference in the odds of metastases (OR 2.18, 95% CI 0.85-5.89) [98].

Promising oncologic outcomes have also been reported for LPN with respect to more complex tumors. Porpilgia et al published a retrospective case series of 100 consecutive patients LPN for tumors ≤ 4 cm and tumors greater than 4 cm, demonstrating that in spite of statistically significant differences in tumor size and location ($p=0.002$), the incidence of positive surgical margins was equivalent and acceptable pathologic results were achieved in both groups [11]. Similarly, a study comparing bilateral OPN to bilateral LPN for bilateral kidney tumors demonstrated equivalent cancer-specific and recurrence-free survival rates in both groups over a mean follow-up of 5.5 years [13].

7. Emerging techniques: Robot-assisted LPN and Laproendoscopic Single-Site (LESS) surgery

Robot-assisted LPN (RPN) has recently been introduced at several centres around the world. In general, its indications are the same as for OPN and LPN[99], and the transperitoneal approach is used most often[18]. Preliminary data suggests that RPN is equivalent to LPN in terms of WIT, perioperative status, and functional outcomes, but the main drawbacks of RPN remain cost and need for trained personnel.

Studies comparing RPN to OPN, comparing RPN to LPN, and investigating the outcomes of RPN for hilar and more complex tumours suggest that RPN is safe, feasible, and provides equivalent functional outcomes to the existing standard procedures [100-103]. In some instances, it also results in a shorter hospital stay [100, 102]. A small study involving 11 patients examined the intra-operative use of indocyanine green to facilitate near infrared fluorescent imaging during RPN. The imaging was used to successfully delineate the renal vasculature in all cases. Interestingly, of the 10 patients with malignancies that were eventually confirmed via histopathology, 7 of these tumors were hyper-fluorescent compared to the surrounding renal parenchyma during the intra-operative imaging [104]. Similarly, Laparoendoscopic Single-Site (LESS) partial nephrectomy is an emerging technique that has been proven feasible for small, exophytic, easily approachable tumors [18]. Further data, prospective studies, and greater surgical experience are needed to truly realize the potential of these emerging technologies.

8. Cost effectiveness

Emerging data suggests that LPN is the most cost-effective procedure for small renal masses. A simulation analysis for cost-effectiveness– based on the case of a healthy 65-year old patient with an asymptomatic, unilateral small renal mass, and using quality adjusted life-years as a measure of benefit– concluded that immediate LPN was the most cost-effective nephron-sparing strategy [105]. In this model, LPN was favorable to OPN, laparoscopic or percutaneous ablation, active surveillance, and nonsurgical management with observation. A direct financial analysis conducted in a retrospective Canadian study demonstrated a lower total hospital cost after LPN (4839 dollars \pm 1551 dollars vs. 6297 dollars \pm 2972 dollars; $p < 0.05$) when compared to OPN [95]. Similarly, a retrospective meta-analysis of 2745 procedures (OPN, LPN, and RPN) confirmed that despite similar OR times, LPN was more cost effective than OPN because of a shorter length of hospital stay. Additionally, despite a longer length of stay compared to RPN, LPN was more cost effective due to lower instrumentation costs [106]. These analyses suggest that LPN currently represents the most economical option with regard to nephron-sparing procedures.

9. Summary

Partial nephrectomy is a standard of care for the surgical management small renal masses. In the past decade, laparoscopic partial nephrectomy has advanced to offer equivalent functional and oncologic outcomes, when compared to open partial nephrectomy and laparoscopic radical nephrectomy, at lower cost. Although the appropriate amount of WIT remains controversial, emerging technology (including hemostatic devices and robotic systems) will continue to facilitate improvement in the surgical management of renal masses.

10. References

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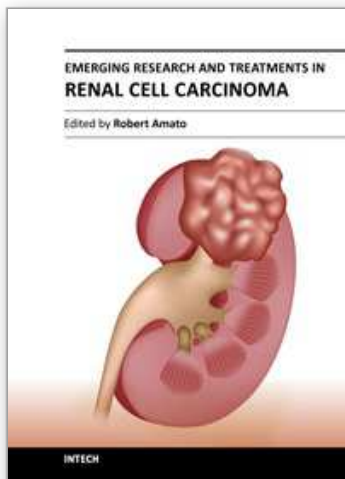
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The field of renal cell cancer has undergone a significant resurgence. This book summarizes up-to-date research and innovative ideas for the future in this rapidly changing field, which encompasses medicine, surgery, radiation oncology, basic science, pathology, radiology, and supportive care. This book is aimed at the clinician or scientist who has an interest in renal cell cancer, whether they are academic or nonacademic. The book covers tumor biology, molecular biology, surgery techniques, radiation therapy, personal testimonies, and present and future treatments of the disease that are on the horizon. The goal was to produce a textbook that would act as an authoritative source for scientists and clinicians and interpret the field for trainees in surgery, medicine, radiation oncology, and pathology.

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