Review Article

Hemostasis in laparoscopic renal surgery

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ABSTRACT

Hemorrhage is a potential risk at any step of laparoscopic nephrectomies (LNs). The advances in surgical equipment and tissue sealants have increased the safety and efficiency of performing LN and laparoscopic partial nephrectomy (LPN). However, hemostasis remains a major issue and there is still scope for further development to improve haemostatic techniques and devices. In this article a literature review of the current methods and techniques of hemostasis was carried out using the MEDLINE®/PubMed® resources. The results of the review were categorized according to the three main operative steps: Dissection, control of renal pedicle and excision of the renal lesion.

Key words: Haemostasis, laparoscopic nephrectomy, partial nephrectomy, review article

INTRODUCTION

Bleeding is a potential risk in renal surgery and can lead to significant morbidity and mortality. In laparoscopic nephrectomies (LNs), the risk of severe hemorrhage is 2.8–5% and this results in a blood transfusion rate of 0.7-6.9%.[1] It is the most common cause for conversion to open procedure and re-exploration, particularly in laparoscopic partial nephrectomy (LPN).[1] Hemorrhage can occur during each step of the operation, from obtaining the pneumoperitoneum right up to the early postoperative period. It can arise from a vascular injury (renal or other vessels), injury to a surrounding structure (particularly the spleen) or as oozing from the renal bed or renal parenchyma.[1] In this article a literature review of the current methods and techniques of hemostasis was carried out using the MEDLINE®/PubMed® resources. The results of the review were categorized according to the main operative steps of LN and LPN: Dissection, control of renal pedicle and excision of the renal lesion. Table 1 summarizes the current methods and techniques used for hemostasis.

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Hemostasis during dissection

Good dissection techniques by using a combination of blunt and sharp methods and identifying the tissue planes are important to avoid unnecessary bleeding. Equally important is the identification and control of vascular structures before cutting, particularly at the renal pedicle and at the upper pole of the kidneys. Hemorrhage even if minimal can obscure laparoscopic vision during dissection, hence meticulous hemostasis is essential. Electrosurgery and Ultrasounic Scalpel are technologies that utilize energy sources to control hemostasis during dissection.[2,3]

In electrosurgery a high-frequency electrical current is used to generate heat, which is applied to cut tissues and to coagulate bleeding vessels. There are two types of diathermy. In monopolar diathermy, the generator can be attached to forceps, scissors or a J-hook and the current flows through the patient to an external plate. The inadvertent thermal injury to the surrounding structures is a well-known risk which could happen as a result of damaged insulation or through contact to another instrument. Bipolar diathermy provides a safer current flow, just between the forceps' jaws.[4] The manufacturers of the advanced bipolar diathermy systems LigaSure™ (Covidien, Boulder, USA) and Enseal® Trio (Ethicon Endo-Surgery) claim they are effective for hemostasis of vessels up to and including 7 mm in diameter.

Ultrasonic or harmonic scalpel is a surgical instrument which uses an energy source to generate ultrasonic waves at a frequency of 55.5 kHz which are conducted to an active blade element for cutting and coagulating tissue. It is composed of a generator, hand piece and blade. The hand piece contains a transducer which consists of piezoelectric ceramic discs which convert electric energy into mechanical motion.

Table 1: Methods and techniques currently used for hemostasis in laparoscopic nephrectomies

Mechanical compression	
Permanent	Sutures, clips, stapler
Temporary	Satinsky clamp, bulldog clamp, grasper
Energy-based technologies	
High-frequency Ultrasound	Harmonic scalpel
Electrosurgery	Monopolar and bipolar diathermy
Lasers	Ho:YAG, KTP
Radiofrequency energy	Habib 4X device
Tissue sealants	
Enzymatic	Fibrin, thrombin
Mechanical scaffolding	Gelatine, oxidized cellulose
Cross-linking	Albumin-gluteraldehyde, cyanoacrylate

The transducer attached to a blade extender transfers the mechanical motion to an active blade which in turn vibrates longitudinally. This vibration has two effects; the first one is to generate heat sufficient for coagulation, the second effect is the mechanical dissection and cavitations which result in cutting. Compared with electrosurgery, harmonic scalpel generates less heat which consequently results in minimal thermal damage, tissue charring, and little smoke, hence a better view of tissue planes and operative field. However, Kim *et al.*, found that the Harmonic ACE® produces very high temperatures (234.5°C) immediately after deactivation which could damage contacted tissue, therefore extra care should be taken during dissection around vital structures.[5] Harmonic scalpel can be used to seal vessels up to the size of 5 mm according to the manufacturer of the Harmonic ACE® (Ethicon Endo-Surgery).

Hemostasis of the renal pedicle

Dissection of the renal blood vessels is a critical step, particularly in laparoscopic donor nephrectomy (LDN) in which longer graft vessel length is preferred. Complex renal vascular anatomy which is defined as two or more renal arteries or veins is common (17-22%) and this can be a challenge to the operator.[1] Failure to achieve or maintain adequate hemostasis at the renal pedicle can lead to catastrophic results; therefore extra care should be taken during dissection, isolation and controlling of the vascular structures at the renal hilum. In LPN, the renal pedicle is usually clamped temporarily by a Satinsky vascular clamp or a bulldog clamp to provide warm ischemia.

There are three methods of securing the isolated renal vessels: Titanium clips, self-locking polymer ligation clips and endoscopic staplers. Hsi *et al.*, reviewed the US Food and Drug Administration (FDA)'s device-related database for these three techniques during LDN between 1992 and 2007, and calculated the estimated overall failure rate for each device, which was 3.0%, 4.9% and 1.7% for staplers, Titanium clips and locking clips respectively.[6]

Endoscopic staplers which provide simultaneous stapling and cutting of the blood vessels had the highest risk of malfunctioning. The two most common mechanisms of failure were inadequate staple lines and failure to release from tissue, and this resulted in the high percentage of severe hemorrhage and open conversion. It was recommended that the staff handling and reloading the devices should be fully trained, and when using the stapler, the operator must use the appropriate vascular jaw width and check that the entire vessel is within the stapler line before firing. It is also vital that the structure to be stapled is not too thick and the device is not fired over other staple lines or clips. Using an articulating or flexible system is advisable when the working space is limited. In the case of failure to release the device the operator should quickly try to gain proximal control with the same or a different technique if sufficient vessel length is available. Endo-staplers are expensive, single-use instruments. One advantage of this device over the other two is its feasibility to be used for en-bloc stapler ligation of the renal vascular pedicles, hence shortening the time of the operation.[7]

Titanium clips were the second most likely to malfunction. Clip malformation, scissoring and the applier getting jammed while firing were the most commonly reported mechanisms of failure, followed by falling of clips off vessels after application. Interestingly, the risk of severe hemorrhage and open conversion were rare. These clips lack a self-locking mechanism and to increase the safety when using them it is advisable to apply multiple clips, avoid further dissection near the clips once applied and to leave a cuff of 1–2 mm on completely dissected vessels.[2,6]

The self-locking, polymer ligation clip system was the most reliable method of hemostasis with the lowest risk of malfunctioning, however, failure results in a significant risk of severe hemorrhage, open conversion and the highest recorded rate of re-operation and death (two cases). Surprisingly, the two most common causes of failure were multiple clips found open during re-operation or dislodgement from vessels during surgery. In May 2011, FDA and the Health Resources and Services Administration (HRSA) issued a contraindication alert for using Hem-o-Lok Ligating Clips for the ligation of the renal artery during LDN, following reports of a further three death cases.[8] Ponsky *et al.*, reviewed the use of Hem-O-Lok clips in 1695 different types of laparoscopic nephrectomies (including 486 donor ones) and reported that none of the clips failed.[9] Sooriakumaran *et al.*, evaluated the risk factors and predictors of the hem-o-lock clip failure *in vitro* and concluded that the clip is safe if at least 1 mm cuff of tissue is left after cutting (particularly in LDN) and if the clip is applied at a perpendicular angle to the vessel.[10] Others recommended visualizations of the locking mechanism around the completely dissected vessel before closure, the use of appropriate-sized clips and placement of at least two clips on the proximal side of the renal vessels before cutting.[6,9]

Hemostasis of the renal parenchyma

Nephron-sparing surgery is becoming the standard procedure for small renal lesions (less than 4 cm). Hemostasis is one of the biggest challenges during this operation due to the high renal blood flow. In order to achieve adequate hemostasis, several techniques and technologies have been used; many of them are still under trial. There are a number of important factors that determine which haemostatic method should be used, such as the tumor size, its site and the depth of penetration in the parenchyma. Currently, there is no standard classification for renal tumors according to the above-mentioned factors. Finley *et al.*, classified renal tumors into Exophytic, Endophytic and Mesophytic according to the percentage of their circumferences which extend beyond the natural border of the kidney (>60, <40 and 40-60 respectively), and Hilar if the tumor is located within 5 mm of the main renal artery or vein.[11]

Hemostatic ischemia

Temporary clamping of the renal vessels allows removal of the renal tumor and the repairing of the parenchymal defect in a relatively bloodless field, however, this method is limited by a short time to minimize the ischemia damage of the remaining nephrons (warm ischemia). Becker *et al.*, reviewed the impact of ischemia time during partial nephrectomy in a multi-centre study, and recommended the restriction of the warm ischemia to 20 min regardless of the surgical approach. If this period of time seems to be exceeded , cold ischemia should be started immediately, and kept ideally within 35 min.[12,13]

LPN without hilar clamping has been described in a number of studies in solitary kidneys and in selective segmental artery clamping.[14,15] Gill *et al.*, recently developed a new technique of Zero ischemia by combining selective branch microdissection of the renal vessels and anesthesia-controlled hypotension which lowers the mean arterial pressure while maintaining good systemic tissue perfusion; the initial results of this new technique were good with average blood loss of 150 ml and no complications related to hypotension.[16] LPN for small exophytic lesions without hilar clamping is also feasible by using a combination of energy-based methods and tissue sealant. Permanent ischemia in the form of regional tissue compression was tried *in vivo* for partial lower pole nephrectomy by using Endoloop suture and pledgeted compression sutures—both these techniques did not provide adequate hemostasis.[17,18]

Excision of the renal lesion

In addition to bipolar diathermy and the harmonic scalpel which were discussed earlier, several technologies utilizing energy have been used in order to achieve hemostasis and minimize the time of warm ischemia.[19] The first haemostatic device used for parenchymal bleeding was Argon beam coagulator (ABC®), a monopolar electrocautery instrument which uses high-pressure flow of the argon gas to clear the surgical field of blood. This was sufficient for minor capillary bleeding but not to control large vessels.[20] The TissueLink® is a high-density monopolar saline-cooled radiofrequency device which provides coagulation and dissection simultaneously.[21] Microwave Tissue coagulator uses a monopolar antenna to coagulate the tissue before excision.[22] In contrast to traditional cold scissors, these techniques can potentially destroy the margins of the incised tissue and lead on the one hand to necrosis and urinary fistula formation, and on the other hand to jeopardizing the assessment of the tumor-free margin. The use of these methods has been limited mainly to assist in hemostasis and excision of very superficial exophytic lesion.

Different types of lasers have been tried in several experimental studies.[23,24] Ho:YAG (Holmium: yttrium, aluminum, and garnet) laser was the first laser used clinically in PLN without hilar clamping in three patients with favorable results (complicated renal cyst, a 2.5-cm renal-cell carcinoma and a non-functioning lower pole in a duplicated collecting system). However, the use of the Ho:YAG laser was associated with excessive smoke accumulation and splashing of blood onto the camera during resection.[25] The clinical use of the KTP (potassium titanyl phosphate) laser and Thallium laser has also been reported more recently in limited cases during robotic partial nephrectomy with or without hilar clamping.[26,27] The problems of smoke evacuation and scatter from the resection site were alleviated by using continuous irrigation during the laser procedure. Compared with the above technologies, radio frequency ablation (RFA) stands out as a promising method of hemostasis, it provides a bloodless plane of coagulative necrosis which can be incised with a sharp instrument.[28] Wu *et al.*, reported using Habib 4X device in 42 cases during robotic clamp-less partial nephrectomy for small lesions, mainly endophytic tumor, their results were comparable with LPN in terms of blood loss, complication rate, renal function and recurrence rate.[29]

Repair of the parenchymal defect (Renorraphy)

This is the most demanding step in LPN. It involves sealing of the breached collecting system and closing the parenchymal defect, and it needs to be performed efficiently within the restricted time of controlled ischemia. This step includes a combination between suturing techniques and tissue sealants.[30,31] The extent and methods of repair depends on the size and the depth of the defect and whether the collecting system is entered or not. Johnston *et al.*, recommended using hilar clamping if the lesion penetrates more than 5 mm into the kidney, and to apply fibrin glue with or without sutured bolster depending on opening of collecting system or injury to renal sinus. (this is more likely if the lesion is within 5 mm of the renal sinus). For a more superficial lesion (less than 5 mm penetration into the kidney) resection with coagulating instruments and fibrin glue is sufficient without hilar clamping.[32]

Suturing is the most reliable method of achieving hemostasis, however, conventional laparoscopic suturing requires advanced laparoscopic skills and is time-consuming in untrained hands. Modifying the suturing techniques by using continuous running suture and eliminating knot tying by using clips such as Lapra-Ty or Hem-o-loks, results in easing and speeding up the parenchymal reconstruction and also enhancing the effectiveness of the hemostasis.[33-35] These techniques are used in both, closing the collecting system and fixing the compressing sutured bolster. Moreover, studies showed that early unclamping of the renal artery after initial parenchymal suturing and before completing the renorrhaphy resulted in reducing the warm ischemia time by almost half.[36,37]

Several types of tissue sealants and haemostatic agents have been in use for many decades.[38,39] They differ considerably in their composition, mechanism of action, ability to seal the collecting system, stability in the urine, and handling.[40,41] Breda *et al.*, reviewed the use of haemostatic sealants during LPN in 18 major academic centers and found that the most commonly used agents were the Surgicel bolster, FloSeal, Tiseel, Glubran and BioGlue.[42] Surgicel bolster was used in all centers except one, followed by FloSeal and Tiseel, while the Glubran and BioGlue were used by a few centers and in combination with at least one of the other agents. Table 2 classifies these agents according to their mechanism of action.

Oxidized cellulose (Surgicel) has a plant origin and was introduced in 1942. It provides a mechanical barrier to bleeding and a stimulus to coagulation. Its haemostatic effect is greater when applied dry. It is an absorbable material and dissolves in two to six weeks. It is characterized by low pH which has an antimicrobial effect, however, it also increases the inflammation of surrounding tissue and can lead to granuloma formation. This granuloma can mimic tumor recurrence on post operative imaging. Its low pH also inactivates the enzymatic agents such as thrombin; hence it cannot be used in conjunction with these agents in one product. It is available as a single sheet or as a cotton-sponge consistency which can be applied on surfaces, or as a tightly knit thick fabric which can be rolled to form sutured bolsters used effectively to achieve hemostasis in large surgical defects when it is combined with suturing and enzymatic sealants.[43]

Gelatin foams have an animal origin and were introduced in 1945. They have a similar mechanism of action as oxidized cellulose and are absorbed completely within four to six weeks. They swell when applied to tissue and can double their volume which enhances the mechanical haemostatic effect; however, this can result in compressive complication if they are applied in confined spaces or near nerves. Gelatin foams can be used dry or wet, and unlike oxidized cellulose they have a neutral pH and therefore can be used in conjunction with thrombin. They are available as a compressed sponge or as a flowable matrix. The latter is used alone (Surgiflo) or with thrombin (FloSeal). Individual comparison studies show no differences in the ability of these two products to achieve hemostasis; however, there has been no clinical trial to testify this.[39]

Thrombin is the most important enzyme in the final common pathway of coagulation. It converts the fibrinogen to fibrin, the building block of a haemostatic plug. Its action depends on the existence of fibrinogen which can be consumed from the patient's own blood in the surgical field or processed from human plasma and combined with thrombin as a fibrin sealant. Thrombin is purified mainly from three sources: bovine, human pooled plasma and recombinant. Bovine-derived thrombin has a risk of allergic reactions and the human-derived one has the risk of blood-borne diseases. The combination between thrombin and gelatin matrix (FloSeal) is one of the most effective products for controlling moderate arterial bleeding in LPN (Laparoscopic partial nephrectomy) ; it needs contact with blood as a source of fibrinogen and can expand up to 20% within 10 min. Gill *et al.*, reported a substantial decrease in procedural and hemorrhagic complications to levels comparable with contemporary open partial nephrectomy by using Floseal.[43]

Fibrin sealants are composed mainly of thrombin and fibrinogen and supplied in separate vials with a dual syringe delivery system which admix these two components immediately before application on the tissue. It acts best when applied to a dry surgical field. There are several different forms of fibrin sealants which vary in their mechanisms to stabilize the fibrin clot: Crosseal contains tranexamic acid as a fibrin stabilizer, Tisseel contains antifibrinolysis aprotinin, and Evicel depends on removal of plasminogen, the enzyme responsible for degradation of fibrin polymers. In Vivostat, the patient's own blood is used to produce autologous fibrin sealants; this eliminates

Table 2: Classification of the commonly used tissue sealants and adhesives

Mechanical scaffold	
Oxidized cellulose	Surgicel
Gelatin	FloSeal*
Enzymatic Agents	
Thrombin	FloSeal*
Fibrin	Tisseel
Cross-linking sealants	
Albumin-gluteraldehyde	BioGlue
Cyanoacrylate	Glubran

*FloSeal is a mixture of bovine-derived Gelatin and human-derived Thrombin the risks of blood-borne diseases and anaphylaxis.[44] Fibrin sealants alone are accepted for superficial parenchymal defects, however, using the combination of other measures as a suturing bolster are more effective when there is a collecting system or renal sinus entry.

Glutaraldehyde-based sealant (BioGlue) is composed of bovine serum albumin and glutaraldehyde. It acts through formation of covalent polymerization between its components and adjacent tissue. It requires a dry field and mixing before delivery to the tissue. It is a synthetic agent and does not require the presence of blood. It usually reaches its maximum strength within 1–2 min and forms hard matrix adherent to the tissue which can avert further suturing or tissue handling and can cause urinary obstruction; therefore it should only be applied after closure of the collecting system. Hidas *et al.*, studied the clinical use of BioGlue and concluded that it was easy to use and safe for sealing the kidney during partial nephrectomy, it provided adequate hemostasis, significantly decreasing the blood loss and transfusion rate, as well as the renal ischemic and operative times.[45]

CONCLUSION

The technique of LN has been evolving since the report of the first case by Clayman *et al.*, in 1990.[46] The advances in surgical equipment and tissue sealants have increased the safety and efficiency of performing LN as well as LPN. However, hemostasis remains a major issue despite several published experimental and clinical techniques. There is still scope for further development of haemostatic devices in order to make LPN the standard of care for small renal tumors.

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