SURGICAL TECHNIQUE

Haemostasis control during laparoscopic partial nephrectomy without parenchymal renorrhaphy: The Vivostat® experience☆


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Abstract

Objective: To present our experience using an autologous fibrin sealant prepared with the Vivostat system® to control haemostasis without any renal parenchymal reconstruction.

Material and methods: We performed 45 laparoscopic partial nephrectomies using this haemostatic agent. The surgical steps were: colon mobilization, identification of ureter, renal vessels and renal tumor, renal artery control with Rummel tourniquet, tumor excision with harmonic scalpel, and application of fibrin glue to the resection bed twice (before and after kidney reperfusion). Patients were evaluated for acute or delayed bleeding.

Results: Mean age was 63.9 years (33–80); mean tumor size was 2.5 cm (1.5–4); mean operative time was 136.1 min (90–180). Mean warm ischemia time was 19.2 min (10–30). Mean blood loss was 97 ml (50–300). Individual haemostatic stitches were performed before application of the sealant if acute bleeding was observed (14 cases). We did not record any case of postoperative bleeding or renal failure. One patient required transfusion due to a big hematoma on the abdominal wall. 65% were clear cell carcinoma, 10% were papillary carcinoma, 20% were oncocitoma. Free margin rate was 100%. Mean hospital stay was 4 days (2–6). Mean follow-up was 14 months (5–45).

Conclusions: Excluding renorrhaphy during laparoscopic partial nephrectomy is feasible and safe. Our initial experience with the vivostat system in laparoscopic partial nephrectomy has been encouraging, but longer follow-up is needed to determine the real benefit of this surgical technique in laparoscopic partial nephrectomy.

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Control de la hemostasia durante la nefrectomía parcial laparoscópica sin reorronfia parenquimatos: la experiencia Vivostat®

**Resumen**

**Objetivo:** Presentar nuestra experiencia en el control hemostático de la nefrectomía parcial laparoscópica utilizando un compuesto de fibrina autóloga (Vivostat system®), sin reconstrucción del parénquima renal.

**Material y métodos:** Hemos realizado 45 nefrectomías parciales utilizando este agente hemostático. Los principales pasos quirúrgicos fueron: decolación, identificación del uréter, hilio y tumoración renal, control de la arteria renal con torniquete de Rummel, exéresis tumoral con bisturí armónico y aplicación del sellador de fibrina en el lecho quirúrgico en 2 fases (antes y después de la reperfusión renal). Se registraron datos de sangrado precoz o diferido.

**Resultados:** Edad media: 63,9 años (33-80); tamaño medio del tumor 2,5 cm (1,5-4); tiempo medio quirúrgico: 136,1 minutos (90-180). Tiempo medio de isquemia caliente 19,2 minutos (10-30). Pérdida sanguínea media: 97 ml (50-300). Se realizaron puntos hemostáticos individuales antes de la aplicación del sellador de fibrina, en caso de sangrado activo importante (14 casos). No se registró ningún caso de sangrado ni fallo renal en el postoperatorio. Un paciente requirió transfusión sanguínea debido a gran hematoma en pared abdominal. El 65% fue carcinoma de célula clara renal, el 10% carcinoma papilar y un 20% fueron oncocitomas. La tasa de márgenes negativos fue del 100%. El tiempo medio de ingreso hospitalario fue 4 días (2-6). El seguimiento medio fue de 14 meses (5-45).

**Conclusiones:** Excluir la reorronfia durante la nefrectomía parcial laparoscópica es posible y seguro. Nuestra experiencia inicial con este sellador de fibrina ha sido positiva, aunque probablemente se necesiten más casos y seguimiento para determinar el beneficio de esta técnica quirúrgica.

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Introduction

Although open partial nephrectomy (OPN) currently remains the standard of care in surgical management of small renal masses, the laparoscopic approach (LPN) represents a feasible alternative to open surgery for single, small, localized renal cell carcinoma. Oncologically comparable to OPN for localized renal masses, most series demonstrate that the LPN is associated with greater warm ischemia time (WIT) and an increased risk of postoperative hemorrhage when compared to OPN.2

Decreased renal function has been associated with diminished survival and increased morbidity in the general medical population, and partial nephrectomy (PN) has equivalent cancer control ability compared to radical nephrectomy (RN). Better renal function preservation associated with PN might be correlated with better survival in patients with renal masses, compared to RN, although in a recently randomized trial comparing PN and RN, a survival advantage was not observed for PN. On the other hand, the duration of the ischemia time has also been described as a factor to predict postoperative renal function.7

Tissue sealants and glues as renal hemostatic agents (HAS) have been used for over 25 years. Over the past 10 years, studies investigating the role of newly emerging renal HAS have shown that they may improve hemostasis and aid in collecting-system repair resulting in fewer complications. In addition, the use of HAS has been proven to be safe during the LPN. The use of HAS and glues is becoming increasingly standardized in most centers performing LPN. Only two previous reports describe the usefulness of autologous fibrin glue using the Vivostat system for laparoscopic partial nephrectomy in a small group of patients.1,2 Currently, it is also used in different surgical settings, including cardiovascular, orthopedic, thoracic and laparoscopic surgery.11

One of the classical surgical steps in open partial nephrectomy is the reconstruction of the renal defect. We describe our technique for achieving effective hemostasis during laparoscopic partial nephrectomy excluding renal parenchymal reconstruction using an autologous fibrin sealant with the Vivostat system.

**Materials and methods**

Between January 2008 and September 2011, we performed 45 laparoscopic partial nephrectomies for single, small-size and exophytic renal lesions. We excluded patients with evidence of tumors greater than 4 cm and venous or lymph node involvement. Abdominal computed tomography scanning was performed in all patients before surgery. Thromboembolic, antiulcerous, and antibiotic profilaxis were administered before all procedures. The operation was performed by the same surgeon in all the procedures (MH).

We used the traditional disposition of trocars for renal surgery: on the left side, parambilical port for the optic (30°), two subcostal trocars (one of them could be 5 mm), and another 5-mm trocar on the iliac zone if it was necessary; the same configuration on the right side except for another subxifoïd 5-mm trocar when the renal mass was on the upper pole and liver separation was needed.
A transperitoneal approach was used in all the procedures. After decollation, the renal pedicle was controlled. Then, the renal mass was individualized and prepared to be excised. In lower pole masses, the ureter was also controlled to avoid urinary injuries. Only the renal artery was clamped utilizing Rummel’s tourniquet (not utilized in 7 cases). The tumor excision was conducted with a harmonic scalpel (ultracision®). An endobag was used to keep the renal mass. Bed resection was inspected for important venous bleeding or urinary injuries; individual stitches were performed only if acute bleeding or collecting system aperture were observed; otherwise, a first application of the fibrin glue was carried out. After 2 min, Rummel tourniquet was cut off, and another layer of the glue was applied. We did not use any parenchymal stitches to reconstruct the renal defect. A drainage was placed in the surgical bed (Fig. 1).

The system is fully automated and consists of three components: an automated processor unit, an automated applicator unit, and a disposable single-patient-use unit, which includes a preparation set and the endoscopic applicator. Details of the biochemical process of the Vivostat™ system have been previously reported.15 It is initiated by biotinbatroxobin, which acts upon the fibrinogen in the patient’s plasma. The completion of the process depends entirely on endogenous thrombin producing a sealant that overcomes the potential infective and antigenic risk. The entire process, from taking the patient’s blood sample until the sealant was ready for use, was fully automated and microprocessor-controlled, generating approximately 5 ml of sealant from 120 ml of the patient’s own blood in approximately 30 min. The anesthetist in the operating room took the blood from an established vascular access line. The fibrin sealant was applied with the use of the laparoscopic applicator immediately after resection of the tumor; the whole resection bed was covered.

Pre-operative and post-operative serum hemoglobin and creatinine, estimated blood loss, warm ischemia time, surgical margins, quantity of fibrin, length of surgery and post-operative bleeding or urine extravasation, ureteral stent introduction, length of hospital admittance, and pathologic report were recorded. A hemorrhagic complication was defined as intraoperative or postoperative bleeding requiring transfusion. Pearson correlation analysis (for continuous variables) was used to identify significant relations between preoperative and postoperative blood and creatinine values.

**Results**

Mean patient age was 63.9 years (range 33–80 years). 27 patients were male and 18 were female. Mean tumor diameter was 2.5 cm (range 1–4 cm). Mean warm ischemia time was 19 minutes (range 10–30 min). Mean fibrin quantity was 5.79 ml (4.1–6.8 ml); 7 patients did not undergo renal artery clampage. In all cases, the entire fibrin sealant was applied. 14 patients needed an individual stitch on the resection bed because of important active venous bleeding. One patient needed an individual stitch on the resection bed because of visualization of urinary defect. No patient needed ureteral stent placement. Hemostasis was immediate in all cases after application of the tissue sealant for 1–2 min in most of the resection site. There were no significant differences between preoperative and postoperative serum hemoglobin (mean 14.9 g/dl [range 13–17.8 g/dl] vs. mean 12.6 g/dl [range 7.9–14.4 g/dl]), and creatinine values (mean 0.91 mg/dl [range 0.75–1.51 mg/dl] vs. 0.95 mg/dl [range 0.62–1.79 mg/dl]; p = ns) (Table 1).

Estimated blood loss ranged from 50 to 300 cm³ (mean, 97 cm³). One patient needed blood transfusion in the postoperative time due to abdominal wall hematoma. Mean operative time was 136.1 min (range 90–180 min). No postoperative bleeding occurred. There was no evidence of urine extravasations or other immediate or delayed complications in any of the forty-five patients after surgery. The histopathologic characteristics of the specimens are reported in Table 1. No positive margins were reported in the pathologic report. Radical nephrectomy was performed in one patient because of intraoperative doubtful margin status without good visualization of tumor limits.

The drainage was removed when the drain loss was lower than 50 cm³/24 h: after 2 days in 39 patients, and

**Figure 1** Main surgical steps: (A) renal artery control with Rummel tourniquet; (B–D) tumor excision with harmonic scalpel; (E) first application of fibrin glue on resection bed; (F) Rummel tourniquet’s withdrawal; (G) second application of fibrin glue after kidney reperfusion; (H) final result.
after 3 days in the other 6. Mean hospital stay was 4 days (2–6). One patient died in the postoperative time due to a cardiologic event (decompensation of hypertrophic myocardioamyloidosis). Mean follow-up time was 14 months (5–45). One patient presented a local relapse with renal venous thrombus, after 18 months of follow-up; open radical nephrectomy could not be performed, and, currently, he is under antiangiogenic therapy. No renal insufficiency was achieved after the follow-up. Following the Clavien–Dindo classification of surgical complications, we have one case of grade II (transfusion) and one case of grade V (death).16

Discussion

We describe our technique for achieving effective hemostasis during laparoscopic partial nephrectomy, excluding renal parenchymal reconstruction and utilizing an autologous fibrin sealant.

Nephron sparing surgery has become the gold standard for small renal masses, since it has shown oncological outcomes equivalent to those of radical nephrectomy while better preserving the renal function. In the general population, chronic kidney disease has been proven to be associated with an increased risk of cardiovascular events and death. Radical nephrectomy has been recognized as a predisposing factor of chronic kidney disease, and it has been suggested to increase cardiovascular events and decrease survival compared to partial nephrectomy in small kidney tumors as well.17,18 Currently, laparoscopic partial nephrectomy has been adeptly wider, since several technical modifications have been introduced, resulting in improved outcomes (hemostasis control and decrease of warm ischemia time).

Kidney reconstruction after tumor excision is one of the main classical steps in this surgery, to hemostasis control and avoidance of urinary fistula. It has been demonstrated that every little nephron counts in renal function, so we tried to show that avoidance of this surgical step is feasible and safe.4 We have undergone tumor excision with harmonic scalpel that allows for an almost total hemostasis of the renal parenchyma; in fact, only 14 patients needed an individual stitch in the resection bed because of venous active bleeding. It is also true that these data are from a selected group of 45 exophytic T1a tumors, but we think that avoidance of parenchymal reconstruction should help in conservation of the renal function. On the other hand, the use of bulky and deep sutures (2–0) into bleeding areas of the renal sinus could promote iatrogenic arteriovenous fistula formation.

There are many factors that influence preservation of the renal function after this surgery such as age and patient’s comorbidities (diabetes, arterial hypertension), warm ischemia time, and tumor size. Old patients with several comorbidities are usually present in our routine practice and a WIT lower than 20 min has not improved functional results, so we have to search other points of technique which could improve renal function after partial nephrectomy. From this point of view, this technique could aid in this

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way, diminishing renal damage, although creatinine values were probably a weak parameter to measure renal function. Longer follow-up is needed to confirm no changes in renal function in our data.

This surgical technique is also promoted to decrease warm ischemia time. Warm ischemia during PN is associated with an increased risk of alteration of renal function and chronic kidney disease. The renal cortex is exquisitely sensitive to warm ischemia, as metabolic activities are predominantly aerobic. Immediately following renal arterial occlusion, adenosine triphosphates begin to break down into monophosphate nucleotides, providing energy for structural and functional cellular integrity. As energy sources become rapidly depleted in an anaerobic environment, cellular membrane transport mechanisms fail, and an influx of salt and water results in cellular edema and death.\textsuperscript{19} Although the maximal safe duration of warm ischemia is controversial, it has been suggested that warm ischemia should be limited to 20–25 min whenever feasible.\textsuperscript{8,19} Several surgical techniques to decrease WIT (on demand clamping,\textsuperscript{20} zero-ischemia,\textsuperscript{21} clamping renal parenchima\textsuperscript{22}) have been described, but WIT lower than 20 min is not associated with clinically relevant functional results.\textsuperscript{23} In our data, the renal artery was clamped in 38 patients (85%), and mean WIT was 19 min, in accordance with the published series (Table 2). We find that hemostasis control with harmonic scalpel during tumor excision and avoidance of renal closure could improve this WIT. As it has been mentioned before, kidney reperfusion is performed after the first application of fibrin glue, so we can reduce WIT for a few minutes.

Several commercially available fibrin tissue sealants (so-called fibrin glues) have been used to assist in hemostasis and collecting system closure during open and laparoscopic partial nephrectomy with apparent clinical success.\textsuperscript{3–13} Although the composition of the component and the methods of preparation vary considerably, their primary components and effects are similar (Fig. 2). A recent review of the Cochrane Database including seven controlled trials suggests that fibrin sealants are efficacious in reducing postoperative blood loss (around 134 per patient) and perioperative exposure to allogeneic red blood cell transfusion (on average by a relative 54%) without any effect on clinical outcomes.\textsuperscript{30} From our knowledge, this is the first time that this fibrin glue has been used in laparoscopic partial nephrectomy without parenchymal reconstruction.
In our opinion, the utilization of harmonic scalpel during tumor excision aids a lot in hemostasis control and allows for avoidance, in the majority of cases, of hemostatic sutures. A good visualization of tumor limits is obtained, so we do not usually use cold scissors in this surgical step. In our experience, intraoperative cold biopsies from the surgical bed are not needed when there is a correct visualization of the tumor limits. On the other hand, the particular laparoscopic applicator of the Vivostat system allows for the solution to spread evenly over the resected bed; thus, small amounts of sealant can be accurately delivered in tissue. The sealant polymerizes on contact and sets over several minutes. This system offers the surgeon a controlled, precise, and efficient means of fibrin sealant application with potential performance advantages over conventional spray application systems.

We acknowledge the limitations of this retrospective study, where 45 selected T1a tumors were included to undergo this technique. In spite of this limitation, however, this study revealed that laparoscopic partial nephrectomy in exophytic T1a tumors is feasible and safe when this technique is utilized. Randomized control studies aimed at investigating the efficacy of hemostatic agents or glues are required, but they may be difficult to perform due to the widespread use of these agents.

Conflict of interest

The authors declare that they have no conflict of interest.

References


