Benefits and shortcomings of superselective transarterial embolization of renal tumors before zero ischemia laparoscopic partial nephrectomy

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Abstract

Aims: To report feasibility, safety and effectiveness of “zero-ischemia” laparoscopic partial nephrectomy (LPN) following preoperative superselective transarterial embolization (STE) for clinical T1 renal tumors.

Methods: We retrospectively reviewed perioperative data of 23 consecutive patients, who underwent STE prior LPN between March 2010 and November 2012 for incidental clinical T1 renal mass. STE was performed by two experienced radiologists the day before surgery. Surgical procedures were performed in extended flank position, transperitoneally, by a single surgeon.

Results: Mean patients age was 68 years (range 56–74), mean tumor size was 3.5 cm (range 2.2–6.3 cm). STE was successfully completed in 16 patients 12–15 h before surgery. In 4 cases STE failed to provide a complete occlusion of all feeding arteries, while in 3 cases the ischemic area was larger than expected.

LPN was successfully completed in all patients but one where open conversion was necessary; a “zero-ischemia” approach was performed in 19/23 patients (82.6%) while hilar clamp was necessary in 4 cases, with a mean warm-ischemia time of 14.8 min (range 5–22).

Mean operative time was 123 min (range 115–130) and mean intraoperative blood loss was 250 mL (range 20–450).

No patient experienced postoperative acute renal failure and no patient developed new onset IV stage chronic kidney disease at 1-yr follow-up.

Conclusions: STE is a viable option to perform “zero-ischemia” LPN at beginning of learning curve; however, hilar clamp was necessary to achieve a relatively blood-less field in 17.4% of cases.

Keywords: Embolization; Kidney neoplasm; Laparoscopic partial nephrectomy; Off-clamp; Zero ischemia

Introduction

Laparoscopic radical nephrectomy is the standard of care for patients with T2 tumors and T1 renal tumors where partial nephrectomy (PN) is technically unfeasible.1

Laparoscopic partial nephrectomy (LPN) is an acceptable alternative even though technically demanding compared to open partial nephrectomy (OPN) for the treatment of T1 renal masses when performed by a skilled laparoscopic surgeon.1

Despite the benefits of improved perioperative outcomes, LPN still remains a technically challenging procedure with a steep learning curve, higher rate of intraoperative complications and longer warm ischemia time (WIT) when compared to OPN with particular reference to larger renal masses.1

Main limitations to a widespread use of LPN remain the intraoperative bleeding control without exceeding the safety threshold of WIT.
Advances in surgical techniques and the use of hemostatic agents have expanded the indications for LPN to more complex renal masses with perioperative and oncologic outcomes comparable with those of LPN performed for smaller lesions. The use of bipolar or ultrasonic-based sealing devices for tumor excision has been reported as an effective option to minimize intraoperative blood loss during “off clamp” MIPN with negligible impact on pathologic evaluation of surgical margin status. A recent review by Simone et al. focused on “zero-ischemia” minimally invasive (MI) PN, assessed key steps and surgical outcomes of described techniques, reported by some Authors with different definitions but sharing the basic principle of minimizing to zero the warm ischemic injury during MIPN.

The evidence summarized in this review supports effectiveness of “off-clamp” MIPN in terms of both oncologic and functional outcomes; nevertheless, off-clamp LPN still remains an underutilized treatment option due to the need of an advanced skill of the entire surgical team.

Preoperative superselective transarterial embolization (STE) has been first described by Gallucci et al. as an option to perform LPN without hilar clamping. With the attempt to start performing LPN with an off-clamp approach we assessed the feasibility, safety and effectiveness of LPN with intraoperative controlled hypotension (CH) following STE in patients with clinically T1 renal tumors.

Materials and methods

Institutional review board approval was obtained before the initiation of this study. We retrospectively reviewed data of 23 consecutive patients, admitted to our department for incidental clinical T1N0M0 renal tumors, who underwent STE prior LPN between March 2010 and November 2012. Demographic, perioperative, functional and oncologic follow-up data prospectively collected in a database were retrospectively reviewed.

Preoperative work-up

Preoperative evaluation included routine blood tests with assessment of estimated glomerular filtration rate (e-GFR), a chest-abdominal CT scan with a detailed assessment of renal vasculature.

Angiographic technique

All patients received prophylactic antibiotic treatment before initiation of angiographic procedure. Moderate sedation was administered.

Via a right femoral approach, a renal artery catheterization of the affected kidney was performed through a 7F RDC Vista Brite Tip IG guiding catheter (J&J Company, Cordis Corporation, 14201 NW 60th Ave. Miami Lakes, FL33014, USA). Subsequently a 0.0035” GT hydrophilic Terumo Glidewire® is forwarded under a continuous saline flush until the proximal third of the renal artery to obtain a selective arteriogram (Terumo Europe N.V., Leuven, Belgium).

Superselective catheterizations of tertiary and quaternary arterial branches supplying the tumors were performed through a Renegade HI-FLO® microcatheter (Boston Scientific International S.A., Nanterre Cedex, France) on 0.014” guidewire.

Embolization was performed using 15–250 μm polyvinyl alcohol Contour SE Microspheres Device (Embosphere®, Boston Scientific International S.A., Nanterre Cedex, France).

Each syringe (total volume of saline and microspheres 5 mL) was mixed with 15 mL of contrast medium (Visipaque; Iodixanol GE Healthcare, Princeton, NJ), to obtain a stable suspension of the microspheres.

A final angiogram was obtained to highlight complete disappearance of tumor vascularity and to assess the ischemic area surrounding the target lesion.

All procedures were performed by two skilled interventional radiologists (D.S., S.C.), who independently assessed the outcome of procedure as follows: 1. “appropriate”, when the extent of ischemic area was almost covering the extent of tumor area; 2. “suboptimal”, when tumor vascularity at final angiogram was still visible; 3. “larger than expected” when the extent of ischemic area was larger than neoplastic area by 20%.

Surgical procedure

LPN was performed 12–15 h following STE. All procedures were carried out with the intent of performing a “zero ischemia” approach by using controlled hypotensive anesthesia as described by Gill et al.

Patients were placed in extended flank position and a transperitoneal approach was used. Pneumoperitoneum was obtained by the Hasson technique. A 3 or 4 port approach was used.

Hilar vessels were selectively identified and isolated.

Renal tumor identification and its isolation was performed, taking care of maintaining a perirenal fat cuff surrounding the tumor.

Before starting tumor dissection, CH was performed in all patients.

When required, a laparoscopic Satinsky clamp was used through a 10 mm port to obtain renal artery occlusion. Tumor enucleation was done by blunt dissection, following the cleavage plane between the tumor and the healthy parenchyma. The specimen was secured into an endobag.

Intraoperative frozen sections were never performed.

The parenchymal defect was closed according to the “sliding clip” renorrhaphy.
Hemostatic agents were selectively applied to accomplish a complete hemostasis. Gerota’s and Toldt’s fascia were closed and a drain was left in the retroperitoneal space in all patients.

**Postoperative work up and follow-up**

Complications were recorded and graded according to the modified Clavien–Dindo system.

Renal function was evaluated with 3-, 6-, and 12-mo serum creatinine levels assessment and e-GFR evaluation according to modification of diet in renal disease (MDRD) formula.9

Follow-up schedule included blood work-up at 3-month intervals, abdominal ultrasound and chest X-ray at 6-mo follow-up and yearly thereafter, and computed tomography (CT) scan at 1-yr follow-up and yearly thereafter.

**Results**

Demographic, perioperative and pathologic data were summarized in Table 1.

The extent of ischemic area was judged by two interventional radiologists as appropriate (Fig. 1), larger than expected (Fig. 2) and suboptimal in 16, 3 and 4 cases, respectively.

After stratifying renal tumors according to R.E.N.A.L. nephrometry score, the extent of ischemic area was appropriate in 100%, 44.4% and 33.3% when nephrometry score was ≤5, 6 and ≥7, respectively (Table 2).

According to Clavien–Dindo classification, 15/23 (65%) patients experienced STE related grade 1 complications (flank pain treated with analgesics). A “zero-ischemia” approach was performed in 19/23 patients (82.6%) while hilar clamp was necessary in 4 cases, with a mean WIT of 14.8 min (range 5–22).

Mean operative time was 123 min (range 115–130) with a mean EBL of 250 mL (range 20–450). According to Clavien–Dindo classification, grade 1, 2 and ≥3 complications occurred in 3 (13.04%; antipyretics-analgesics use), 2 (8.69%, blood transfusions), and 0 patients, respectively. Accidental renal mass disruption occurred in 3 cases despite a blunt approach to dissection plane. Mean postoperative hemoglobin levels were 11.5 g/L (range 9.1–13.6).

Final pathology revealed renal oncocytomas in 4 cases (17.39%), pT1a and pT1b renal cell carcinomas in 11 (47.82%) and 8 (34.78%) cases, respectively.

All patients had negative surgical margins at final pathology. No patient experienced postoperative acute renal failure; median e-GFR at baseline (94 ml/min, IQR 72–110) and at discharge (89 ml/min, IQR 75–105) were not statistically significant (Chi-square test; p = 0.28). No patient developed new-onset IV stage Chronic Kidney Disease (CKD) at 1-yr follow-up. At 1-yr follow-up neither local nor distant recurrences were observed.

**Discussion**

Renal artery embolization is today considered a safe angiographic procedure in a variety of clinical scenarios, including preoperative as well as postoperative and palliative settings.10,11

It is today recognized by the European Association of Urology guidelines as an effective palliative treatment option for patients with renal tumors unfit for surgery and suffering from massive hematuria or flank pain,1 where the benefits of renal artery embolization before radical nephrectomy for patients renal cell carcinomas with inferior vena cava thrombus have been questioned.

With regard to specific complications of transarterial embolization of renal artery, as well as of segmental branches of renal artery, coil migration is a rare (<2% of cases) although potentially severe event with permanent sequelae; with growing experience in this field, its
occurrence can be significantly reduced and restored using endovascular grasping devices.12

More rare complications of this angiographic procedure, although potentially life-threatening, include unintentional non-target embolization that can result in spine, lower extremity, and bowel infarction,13–16 groin hematomas in less than 2% of patients following renal artery embolization,11,12 and, very rarely, infection related to renal artery embolization.12

STE is a recognized and widely used salvage procedure in patients experiencing postoperative bleeding following PN. Although potentially life-threatening, this is a rare (1–2%) event, occurring 2–3 weeks following surgery, usually triggered by either a bleeding pseudoaneurysm or an artero-venous fistula along the renal stump.17

In the preoperative setting of patients with small renal masses selected for PN, STE was first described by Galuzzi et al. in 2007 as the first step of off-clamp LPN.15

Subsequently, Simone et al. reported mid-term outcomes of 1107 and later in 210 consecutive patients with moderate nephrometry score renal tumors from the same center.18

In this large series with long follow-up, the Authors reported a negligible incidence of procedure-specific complications, highlighting the benefits of a significant reduction of intraoperative blood loss despite a straight approach to renal tumor without any care of hilar vessels (neither isolation nor clamping).

The reported incidence of Clavien ≥3a complications in this series was 5.7%, the loss of renal function at early and late evaluations were negligible and oncologic results were comparable to those available in Literature.18

Later, Rais-Bahrami et al. performed a retrospective data analysis comparing the outcomes of 126 and 264 patients who underwent off-clamp and hilar clamp LPN, respectively. In this series, the complication rate of off-clamp

Figure 1. Preoperative CT scan (A); renal arteriogram (B); superselective catheterization of quaternary order artery feeding tumor [blue line surrounding the tumor] (C); final angiogram showing appropriate extent of ischemic area [surrounded by the blue line] (D).
group compared favorably with hilar-clamp group, and the Authors highlighted the improved functional outcomes (6 mo percent change in serum creatinine levels) achievable with off-clamp LPN compared to conventional on-clamp LPN group ($p = 0.04$).  

In 2011 Gill et al. introduced the term “zero ischemia” PN, reporting a preliminary experience of MIPN performed under CH as a viable option to avoid hilar clamping.  

Later, Gill et al. reported “zero-ischemia anatomical partial nephrectomy”, an off-clamp MIPN performed with a superselective microdissection of tertiary and quaternary arterial branches feeding the tumor without the use of controlled hypotensive anesthesia.  

This technique has the same rationale of STE: obtaining an intraoperative superselective control/occlusion of small arteries directly supplying the tumor without the need of performing a preoperative angiographic procedure.  

Although this technique has demonstrated its feasibility and effectiveness in expert hands, it remains a technically demanding procedure requiring an advanced skill of the entire surgical team in the field of MIPN.  

In this manuscript we report a preliminary experience on STE before “zero ischemia” LPN: our technique is a hybrid technique combining the preoperative angiographic procedure to a cautious use of CH during LPN. Both these techniques were applied to provide us a “parachute effect” in order to minimize intraoperative arterial bleeding at the beginning of the learning curve while allowing us to accomplish MIPN with an off-clamp approach.  

In our experience, the hybrid combination of CH and STE provided effective bleeding control in most cases and allowed us to perform LPN in an “unclamped” fashion in 19/23 (82.6%) patients. Besides, no specific procedure related complications occurred except for a mild degree
postoperative embolization syndrome in 15/23 (65%) patients and renal function preservation was demonstrated as in the early as well as in the late follow-up (1-yr e-GFR) evaluation.

Despite these benefits, in our experience STE demonstrated several shortcomings.

Firstly, although feasible in “expert hands”, an effective intraoperative bleeding control during LPN following STE was hard to achieve in about 20% of cases where arterial clamping was necessary to ensure an adequate hemostasis and certain negative surgical margins.

As reported in the Results section, the negative correlation between increasing R.E.N.A.L. nephrometry score and the achievement of an appropriate extent of ischemic area with STE has to be considered as an intrinsic limitations of this procedure, especially in challenging settings (larger and/or endophytic tumors), when a complete occlusion of arterial feeders with STE would have a stronger rationale.

Besides, neither STE nor CH impact on venous back-flow which sometimes affects the tumor resection and often requires a temporarily increase of pneumoperitoneum pressure.

With regard to achievement of negative surgical margins, in three cases we experienced an accidental incision of the correct cleavage plane between the tumor and the healthy parenchyma.

Some concerns about the reproducibility of preoperative STE include the potential risks of non-target embolization, as well as the risk of an ischemic area larger than desirable, which accounted for 3/23 cases in our series (13%). However, this finding did not turn in a clinically significant renal function loss.

When comparing our experience with findings previously reported by Simone et al.,18 we acknowledge that some shortcomings highlighted in our experience may be consequent to the lack of an institutional protocol able to guarantee to patients a straight access to surgical procedure immediately following STE.

This limitation of our protocol could account for the high incidence of postoperative embolization syndrome, the tissue fragility due to the edema and necrosis that may negatively impact on the achievement of negative surgical margins.

Finally, detractors of STE consider this preoperative step as an adjunctive invasive procedure requiring a skilled interventional radiologist; notwithstanding, a rare (1–2%) but life-threatening complication of PN is the delayed bleeding, usually occurring 2–3 weeks after surgery due to a pseudoaneurysm or to an artero-venous fistula along the renal stump.

Since the first option treatment for these patients is the STE of these vascular lesions, a dedicated team of interventional radiologists should be considered as a cornerstone in centers performing either OPN or MIPN.

In conclusion, STE prior MIPN may be considered as a safe option, especially for surgeons at beginning of their learning curve who want to face LPN without hilar clamp, while, with increasing experience in the field of MIPN, a skilled surgical team may consider to face off-clamp MIPN without the need of preoperative STE.20

Finally, keeping in mind the shortcomings of STE described above, we believe that this technique may also be an option for complex scenarios, such as imperative MIPN for tumors with high nephrometry score, where an optimal control of intraoperative bleeding may contribute to the maximal preservation of renal function.

Conflict of interest statement

All Authors disclose any financial and personal relationships with other people or organizations potentially biasing this study.

References