Original Article

Intraoperative ultrasound control of surgical margins during partial nephrectomy

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Abstract

Aims: To evaluate a simple and fast technique to ensure negative surgical margins on partial nephrectomies, while correlating margin statuses with the final pathology report.

Subjects and Methods: This study was conducted for patients undergoing partial nephrectomy (PN) with T1–T2 renal tumors from January 2010 to the end of December 2015. Before tumor removal, intraoperative ultrasound (US) localization was performed. After tumor removal and before performing hemostasis of the kidney, the specimens were placed in a saline solution and a US was performed to evaluate if the tumor's capsule were intact, and then compared to the final pathology results.

Results: In 177 PN(s) (147 open procedures and 30 laparoscopic procedures) were performed on 147 patients. Arterial clamping was done for 32 patients and the mean warm ischemia time was 19 ± 6 min. The mean US examination time was 41 ± 7 s. The US analysis of surgical margins was negative in 172 cases, positive in four, and in only one case it was not possible to conclude. The final pathology results revealed one false positive surgical margin and one false negative surgical margin, while all other margins were in concert with US results. The mean tumor size was 3.53 ± 1.43 cm, and the mean surgical margin was 2.8 ± 1.5 mm.

Conclusions: The intraoperative US control of resection margins in PN is a simple, efficient, and effective method for ensuring negative surgical margins with a small increase in warm ischemia time and can be conducted by the operating urologist.

Key Words: Kidney cancer, nephron-sparing surgery, partial nephrectomy, surgical margins, ultrasound

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INTRODUCTION

For localized kidney neoplasms; partial nephrectomy (PN) was restricted to imperative indications (patients with a single kidney, renal insufficiency, or bilateral tumors).[1]

PN has shown similar oncological results to radical nephrectomies with decreased overall and noncancer-related mortality rates,[2] allow for renal function preservation,[3] and decrease the need for dialysis and transplantation.[4]

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Several studies have shown that surgical margins of <1 cm do not yield a higher recurrence rate as long as tumors are completely excised.[5]

We assessed a technique for evaluating surgical margins during PN(s) that minimizes the incidences of positive margins, using ultrasound (US).[6,7]

SUBJECTS AND METHODS

A prospective study was conducted with retrospective data analysis of all patients having undergone PN for T1–T2 renal tumors from January 2010 to the end of December 2015.

PN(s) were performed through open, laparoscopic or robot-assisted laparoscopic approaches. Before tumor removal, the operator conducted intraoperative US localization of the tumor with a US (2202; BK Medical, Herlev, Denmark). High-frequency probes used were:

- BK Medical 8815-RF; 5–12 MHz for open surgery,
- BK Medical 8666-RF; 5–12 MHz for laparoscopic surgery.

The tumor was removed with the standardized minimal healthy tissue margin technique. After resection and immediately before performing hemostasis, US control of the surgical margins was performed:

- In the open surgery, PN the specimen was immersed in a saline solution and a sequential US was performed to evaluate in three dimensions if the tumor's capsule was intact
- In the laparoscopic approaches the specimen was placed into a laparoscopic endobag (EB-200; Brightness Medical, Jiangsu, China) filled with enough saline solution to cover the specimen. The laparoscopic US probe was then placed into the endobag and an US was performed. The saline bath was then aspirated, and the endobag immediately closed to avoid cancer cell spillage, and the bag was placed in the lower abdomen part. We did not require an extra trocar for the US probe.

In both open and laparoscopic PN(s), the urologist surgeon performed the US. If the margins were negative, hemostasis was performed. If not, an extra rim of renal parenchyma was removed circumferentially to include the entire remaining margin. The size was adapted to US disruption aspect of the capsule. US time duration was measured during the specimen margins control. A blind pathology evaluation of the specimens was conducted, with the pathologist not knowing the US results. The 2009 TNM staging system was used: R0 for no residual tumor at the margin, R1 for microscopic residual tumor at the margin, and R2 for macroscopic residual tumor at the margin. Intraoperative US results were correlated with the final pathological margin status results. Snap frozen section analysis was not performed.

RESULTS

In 177 PN(s) on 147 patients were included (seven patients were operated bilaterally, and 17 had multifocal tumors on the same kidney). Patients' characteristics and data are described in Table 1.

Open surgery was performed in 144 PN(s) and 30 by laparoscopic approaches (20 laparoscopy and 10 robot-assisted laparoscopy).

Hilar clamping was done in 32 cases with a mean warm ischemia time of 19 ± 6 min. Parenchymal clamping was done in 48 procedures and clamping was not needed in 74 cases. Mean operative time was 112 ± 31 min and the mean estimated blood loss was 230 ± 160 ml.

US control of surgical margins of the specimens was positive in four patients. As described above these patients had an extra rim of renal parenchyma resected. Mean US examination time was 41 ± 7 s. In only one case, the US control was not possible because no capsule was visible.

The pathology data are described in Tables 2 and 3.

Table 1: Patients characteristic

Patients characteristic	No.
Gender: Male/female (*n*)	93/54
Mean age ± SD (years)	66 ± 10
Mean BMI ± SD (kg/m^2)	26 ± 5
ASA score: 1/2/3 (*n*)	33/74/40
Previous abdominal surgery (*n*)	74
Previous history of smoking (*n*)	78

SD: Standard deviation, BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 2: Histological results

Patients characteristic	No.
Mean tumor size ± SD (cm)	3.53±1.43
Mean margin size ± SD (mm)	2.8±1.5
TNM classification	
pT1a	112
pT1b	55
pT2	8
pT3	2

SD: Standard deviation

Table 3: Pathological assessment

Pathological assessment	No. of PNs
Clear cell carcinoma	138
Papillary carcinoma	15
Chromophobe carcinoma	6
Angiomyolipoma	4
Oncocytoma	14

Pathology final results showed:

- All except one negative US surgical margins were confirmed
- Among the positive US surgical margins all except one were confirmed
- In the case where US determination was not feasible, the surgical margins were negative.

In addition, all final surgical margins were negative, even if an extra rim resection of renal parenchyma was needed.

Intraoperative US determined margin status with 99% sensitivity and 75% specificity. Positive and negative predictive values were respectively 99% and 75%.

DISCUSSION

Recent studies[8,9] have shown that, although the tumor might not be completely removed by PN, as in R1 cases, overall and cancer specific survival rates seem to be comparable to those in R0 cases, with a higher recurrence rate. However, until studies with long-term follow-up are published, it makes sense to remove a tumor entirely.

This study was aimed at evaluating and validating a technique for evaluating surgical margins in PN specimens.

Intraoperative US in PN was discussed in previous studies as a control technique of the surgical margins but was not done on the specimen. Polascik *et al*.[10] studied intraoperative US in open PN. One-hundred patients undergoing PN were evaluated intraoperatively by US. Surgical margin evaluation was directly performed on the resected kidney with no specimen analysis. Among the 100 patients, eight had a radical nephrectomy because US showed an extensive tumor, three patients avoided surgery since the intraoperative US demonstrated benign cysts while malignancy was first suspected. US was used to ensure the negativity of surgical margins in four out of 40 patients in whom intraoperative gross pathological evaluation confirmed tumor at the margin. In the four cases, a one cm tumor-free margin was excised under US guidance, and the pathological analysis revealed normal parenchyma. This study shows that intraoperative US was efficient and reliable for intraoperative accurate evaluation and management of the surgical margins in the operated kidney.

Nguyen *et al*.[11] developed a technique in which the deep tumor margins were marked by a needle implanted *in situ* under US guidance. In a group of four patients, one patient had a grossly positive deep margin because of improper needle placement. The specimens were not evaluated by US in their study.

We demonstrated here that missed positive margins could be easily evaluated and detected by performing intraoperative US on the specimen to evaluate the surgical margins after resection.

In a study on 41 patients undergoing open PNs, the surgical margins of the specimens were controlled *ex vivo* by US.[6] Thirty-eight cases had negative margins, one case could not be done due to technical failure, and two cases had positive surgical margins, and an extra resection was done. The pathology results for these extra resections were negative in one case (false positive) and an R1 positive margin in the other case which was totally removed in the extra resection. US sensitivity and specificity were 100% and 97%, respectively. Other study was done on 12 patients who underwent laparoscopic PN:[7] the surgical margins of the specimens were controlled intracorporeally by US before performing the hemostasis. Eleven cases had negative margins, and one case had positive surgical margins, and an extra resection was made. The pathology results for this additional resection were negative (false positive). US sensitivity was 100%. In both studies, US results were well correlated with the final pathological results. However, these studies were limited by the small number of included patients.

Intraoperative US was widely used in breast cancer-sparing surgery to confirm complete tumor excision and rule out macroscopic invasive ductal carcinoma at the surgical margins.[12,13] A study done on 46 surgical specimens showed excellent results with a negative predictive value of 100%.[14] However, one of the limitations was the risk of underestimating the size of the healthy rim of tissue around the excised tumor due to specimen compression while performing the US with the so-called "pancake phenomenon." It results in an increased rate of false positive specimens and unnecessary repeat excision. That is why our specimens were immersed in a saline solution to minimize compression applied to the tumor.

Hagemann and Lewis[15] retrospectively reviewed 163 cases of intraoperative frozen section analyzed during PN. In 112 cases, the pathologist detected 12 of the 16 positive margins (four false-negative results) with a sensitivity of 75%.

Intraoperative frozen section analysis was noted by Kubinski *et al*.[16] as an unnecessary expense without providing reliable information. Intraoperative frozen section did not correlate well with final pathology results in a multi-institutional survey.[17] However, it was seen by others as a useful and reliable tool to ensure margin negativity in PN.[18,19]

In a laparoscopic approach, it is impossible to analyze frozen sections of the tumor without loss of the pneumoperitoneum during specimen extraction.

If the extraction is performed before hemostasis, the decrease in abdominal pressure can lead to increase bleeding. If hemostasis is done before specimen extraction, positive margins of the frozen section analysis will require a reclamping, sutures

removal, and an extra rim of renal parenchyma resection, which can be noxious for the kidney and time consuming. In this technique, a pneumoperitoneum loss can be avoided by performing intracorporeal US in a laparoscopic PN. The duration of US control was short and can be done immediately after the removal of the tumor and before hemostasis.[7]

Another advantage of this technique is to shorten the procedure in comparison to the frozen section analysis.

Timsit *et al*.[20] reported excellent results with tumor margins macroscopically evaluated by the surgeon during PN in 61 cases with a 100% sensitivity and 96% specificity.

However, intraoperative US control for specimen surgical margins has advantages over an evaluation by the operator eyes. US results can be easily documented. The tumor's capsule is readily identifiable by US due to its peritumoral hypoechoic halo and US of the resected specimen is an accurate tool. Finally, manipulation and cutting of the specimen before inking is avoided by using US. However, randomized controlled study is needed to determine which technique is more accurate.

CONCLUSIONS

We confirm in this study the efficiency and effectiveness of an original and simple method for ensuring negative surgical margins during PN. The increase in warm ischemia is minor. The procedure was easily performed by the surgical operator. Correlation with final pathology results of surgical margins was high.

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Conflicts of interest
There are no conflicts of interest.

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