EUROPEAN UROLOGY 64 (2013) 314–322

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Endo-urology

Laparoendoscopic Single-site Partial Nephrectomy: A Multi-institutional Outcome Analysis

Francesco Greco [a,], Riccardo Autorino [b], Koon H. Rha [c], Ithaar Derweesh [d], Luca Cindolo [e], Lee Richstone [f], Thomas R.W. Herrmann [g], Evangelos Liatsikos [h], Yinghao Sun [i], Caterina Fanizza [j], Udo Nagele [k], Jens-Uwe Stolzenburg [l], Soroush Rais-Bahrami [f], Michael A. Liss [d], Luigi Schips [e], Ahmad Kassab [b], Linhui Wang [i], Panagiotis Kallidonis [h], Zhenjie Wu [i], Shin Tae Young [c], Nasreldin Mohammed [a], Georges-Pascal Haber [b], Christopher Springer [a], Paolo Fornara [a], Jihad H. Kaouk [b]*

[a] *Department of Urology and Renal Transplantation, Martin-Luther-University, Halle/Saale, Germany;* [b] *Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH, USA;* [c] *Department of Urology, Yonsei University College of Medicine, Seoul, South Korea;* [d] *Division of Urology, University of California San Diego, La Jolla, CA, USA;* [e] *Urology Unit, S. Pio da Pietrelcina Hospital, Vasto, Italy;* [f] *The Arthur Smith Institute for Urology, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY, USA;* [g] *Department of Urology and Urological Oncology, Division of Endourology and Laparoscopy, Hannover Medical School, Hannover, Germany;* [h] *Department of Urology, University of Patras, School of Medicine, Patras, Greece;* [i] *Department of Urology, Changhai Hospital, Shanghai, China;* [j] *Department of Clinical Pharmacology and Epidemiology, Consorzio Mario Negri Sud, Santa Maria Imbaro, Italy;* [k] *Department of Urology, LKH, Hall i. Tirol, Austria;* [l] *Department of Urology, University of Leipzig, Leipzig, Germany*

Article info

Article history:
Accepted January 22, 2013
Published online ahead of print on February 8, 2013

Keywords:
Laparoendoscopic single-site surgery
Partial nephrectomy
Warm ischemia time
Complications

Abstract

Background: Laparoendoscopic single-site surgery (LESS) has been developed in an attempt to further reduce the surgical trauma associated with conventional laparoscopy. Partial nephrectomy (PN) represents a challenging indication for LESS.
Objective: To report a large multi-institutional series of LESS-PN and to analyze the predictors of outcomes after LESS-PN.
Design, setting, and participants: Consecutive cases of LESS-PN done between November 2007 and March 2012 at 11 participating institutions were included in this retrospective analysis.
Intervention: Each group performed LESS-PN according to its own protocols, entry criteria, and techniques.
Outcome measurements and statistical analysis: Demographic data, main perioperative outcome parameters, and perioperative complications were gathered and analyzed. A multivariable analysis was used to assess the factors predicting a short ($\leq$20 min) warm ischemia time (WIT), the occurrence of postoperative complication of any grade, and a *favorable outcome*, arbitrarily defined as a combination of the following events: short WIT plus no perioperative complications plus negative surgical margins plus no conversion to open surgery or standard laparoscopy.
Results and limitations: A total of 190 cases were included in this analysis. Mean renal tumor size was 2.6, and PADUA score 7.2. Median operative time was 170 min, with median estimated blood loss (EBL) of 150 ml. A clampless technique was adopted in 70 cases (36.8%), and the median WIT was 16.5 min. PADUA score independently predicted length of WIT (low vs high score: odds ratio [OR]: 5.11 [95% confidence interval (CI), 1.50–17.41]; $p = 0.009$; intermediate vs high score: OR: 5.13 [95% CI, 1.56–16.88];

* Corresponding author. Department of Urology and Kidney Transplantation, Martin-Luther-University, Ernst-Grube-Strasse 40, 06120 Halle/Saale, Germany.
E-mail address: francesco.greco@medizin.uni-halle.de (F. Greco).

http://dx.doi.org/10.1016/j.eururo.2013.01.025

$p = 0.007$). The overall postoperative complication rate was 14.7%. The adoption of a robotic LESS technique versus conventional LESS (OR: 20.92 [95% CI, 2.66–164.64]; $p = 0.003$) and the occurrence of lower ($\leq$250 ml) EBL (OR: 3.60 [95% CI, 1.35–9.56]; $p = 0.010$) were found to be independent predictors of no postoperative complications of any grade. A favorable outcome was obtained in 83 cases (43.68%). On multivariate analysis, the only predictive factor of a favorable outcome was the PADUA score (low vs high score: OR: 4.99 [95% CI, 1.98–12.59]; $p < 0.001$). Limitations of the study were the retrospective design and different selection criteria for the participating centers.

Conclusions: LESS-PN can be safely and effectively performed by experienced hands, given a high likelihood of a single additional port. Anatomic tumor characteristics as determined by the PADUA score are independent predictors of a favorable surgical outcome. Thus patients presenting tumors with low PADUA scores represent the best candidates for LESS-PN. The application of a robotic platform is likely to reduce the overall risk of postoperative complications.

1. Introduction

Currently available evidence suggests that localized kidney cancer is best managed by nephron-sparing surgery (NSS) whenever technically feasible [1]. Open partial nephrectomy (PN) still represents the gold standard NSS procedure. Laparoscopic PN (LPN) has also gained popularity but is currently performed in a few high-volume reference centers, and its diffusion has been limited by the steep learning curve [2]. Conversely, robotic assisted LPN is gaining momentum as a promising procedure that is able to bridge the technical difficulties of LPN in favor of broader diffusion of minimally invasive NSS [3].

Since its early use in urology, there has been a growing interest in laparoendoscopic single-site surgery (LESS), which has proved to be applicable in the clinical field, being safe in the hands of experienced laparoscopic surgeons in well-selected patients. The spectrum of extirpative and reconstructive urologic procedures with LESS has been described to date [4,5]. LESS-PN was first reported in 2009, with the description of both laparoscopic and robotic approaches [6,7]. A recent literature review showed that at least 110 cases have been reported by selected centers, with a very careful selection of cases [8]. The occurrence of severe complications has been generally low (5.4%), but additional trocars have been added in a high percentage of the cases.

LESS-PN intuitively represents a very challenging procedure because of the potential need for hilar clamping and extensive suturing and for the increased risk of perioperative complications [4,9]. A collaborative multi-institutional project on LESS in urologic surgery was reported about 2 yr ago with the purpose of reporting the contemporary practice of LESS at institutions pioneering the development of this technique in urology [5]. Following that same collaborative effort, the objective of the present study was conceived and initiated to specifically analyze the outcomes of LESS-PN and to identify the predictors of a good surgical outcome for this procedure.

2. Patients and methods

2.1. Study design

Our cohort consisted of consecutive patients treated with LESS-PN based on a clinical diagnosis of enhancing renal mass between November 2007 and March 2012 at 11 participating institutions. Each group performed the procedures according to its own protocols, entry criteria, and techniques. All patients consented specifically to LESS. Raw data without any identifier were retrospectively collected and gathered into a standardized datasheet, which was specifically built for study purposes.

2.2. Outcome

The following information was collected: age, gender, body mass index (BMI), pre- and postoperative renal function, prior abdominal surgery, specific comorbidities as well as American Society of Anesthesiologists (ASA) score and Charlson comorbidity index score, tumor stage and grade, surgical margin status, operative time, warm ischemia time (WIT), and estimated blood loss (EBL).

Additional collected data included type of surgery (robotic LESS [R-LESS] vs conventional LESS [C-LESS]), surgical approach (transperitoneal vs retroperitoneal), access site (umbilical vs extraumbilical), use of ancillary needlescopic or minilaparoscopic ports, preoperative and postoperative serum hemoglobin levels, transfusion data, conversion to open surgery or standard laparoscopy, length of stay, postoperative pain evaluated based on a visual analog scale (VAS) score at discharge, and incision length.

The conversion to open surgery was considered a complication, whereas the conversion to standard laparoscopy by the use of more than one additional trocar was not. Both medical and surgical complications occurring at any time after surgery were captured, including during inpatient stay as well as in the outpatient setting. Complications were classified as early (onset: <30 d), intermediate (onset: 31–90 d), or late (onset: >90 d), depending on the date of onset. All complications were recorded with a grade assigned according to the modified Dindo-Clavien classification [10]. The PADUA score was used to assess the characteristics of the tumors [11].

The function of the kidney was evaluated by measuring serum creatinine and estimated glomerular filtration rate (eGFR) and calculated preoperatively and postoperatively and at 6-mo follow-up using the Modification of Diet Renal Disease equation. Moreover, chronic kidney disease (CKD) of each patient was defined in stages according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative.

Length of follow-up was calculated from the date of surgery to the date of the most recent documented examination.

2.3. Statistical analysis

Patients' baseline characteristics and surgical outcomes were reported as frequencies (percentages) for categorical variables and as median and interquartile range (IQR) for continuous ones.

Three analyses were conducted. The first determined the factors predictive of WIT <20 min and included only the 120 cases in which hilar

clamping was used. The second determined factors predictive of no postoperative complication of any grade (positive outcome). The third determined factors predictive of a *favorable outcome* for LESS-PN, defined as a combination of the following events: WIT <20 min plus no perioperative complications plus negative surgical margins plus no conversion to open surgery or standard laparoscopy.

The above-reported outcomes were first analyzed according to patient characteristics by univariate analysis. To control simultaneously for the possible confounding effects of the different variables, a stepwise logistic regression approach was used for multivariate analysis. In both univariate and multivariate analyses, results are expressed as odds ratios (ORs) with their 95% confidence intervals (CIs). The covariates tested were different depending on the analyzed outcome.

The signed rank test for dependent populations was used to compare *median* levels of creatinine and eGFR at different time points (preoperative, discharge, and 6 mo). Moreover, the rates of patients in CKD stages 1–2 versus stages 3–5 were compared at the different time points (preoperative, postoperative, and 6 mo) by using the McNemar test for paired proportions. Calculated p values were adjusted using the Bonferroni method.

For all statistical analyses, a two-sided p value <0.05 was considered statistically significant. All analyses were performed using SAS Statistical Package Release 9.2 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Study population

Table 1 summarizes the clinical and pathologic characteristics of the 190 patients evaluated in the present study. Table 2 reports the anatomic and topographic aspects of the treated tumors. Patient population was generally young (median age: 55 yr [IQR: 48–64]), non-obese (median body mass index [BMI]: 25.76 kg/m^2 [IQR: 23.53–27.97]), and healthy (median preoperative ASA score: 2 [IQR: 1–3]; Charlson comorbidity index score: 2 [IQR 0–6]). Forty-six patients (24.2%) had a prior abdominal surgery. Mean renal tumor size was 2.6 ± 0.9, and mean PADUA score was 7.2. Median follow-up was 17.28 mo (IQR: 6.43–25.18).

Table 1 – Clinical and pathologic characteristics at baseline

Continuous variables	Median	IQR
Age	55	48–64
BMI	25.76	23.53–27.97
Preoperative creatinine	0.9	0.74–1.03
Preoperative eGFR	85.4	72.95–96.99
Categorical variables	**Patients**	**%**
Gender		
Males	109	57.37
Females	81	42.63
ASA score		
1	84	44.21
2	79	41.58
3	27	14.21
Charlson comorbidity index		
0–1	91	47.89
2–3	61	32.11
≥4	38	20.00
ECOG PS		
0	165	86.84
1	25	13.16
Tumor Side		
Left	89	46.84
Right	101	53.16
Prior surgery		
No	144	75.79
Yes	46	24.21

ASA = American Society of Anesthesiologists; BMI = body mass index; ECOG PS = Eastern Cooperative Oncology Group performance score; eGFR = estimated glomerular filtration rate; IQR = interquartile range.

Table 2 – Tumor anatomic characteristics according to PADUA score

Category	Patients	%
Histology		
Benign	39	20.53
Malignant	151	79.47
Longitudinal (polar) location		
Inferior pole	77	40.53
Upper pole	38	20
Middle pole	75	39.47
Exophytic rate		
>50%	119	62.63
<50%	66	34.74
Endophytic	5	2.63
Renal rim		
Lateral	138	72.63
Medial	52	27.37
Sinus involvement		
No	145	76.32
Yes	45	23.68
UCS involvement		
No	114	60
Yes	76	40
Face		
Anterior	131	68.95
Posterior	59	31.05
Dimension		
≤4 cm	165	86.84
>4 to ≤7 cm	21	11.05
>7 cm	4	2.11
PADUA score		
Low (6–7)	94	49.47
Intermediate (8–9)	62	32.63
High (≥10)	34	17.89

UCS = urinary collecting system.

3.2. Surgical technique and outcomes

Surgical technique and outcomes are shown in Table 3. Median operative time was 170 min (IQR: 130–209), with a median EBL of 150 ml (IQR: 80–300). A clampless technique was adopted in 70 cases (36.8%), and the median WIT was 16.5 min (IQR: 0–26). In 117 cases (61.6%), the surgeons required additional ports, with a standard laparoscopy and open surgery conversion rate of 5.8% (11 of 190 cases) and 2.1% (4 of 190 cases), respectively. The reasons for the conversion to standard laparoscopy were difficulties during dissection and exposure (four cases), demanding suture (five cases) and bleeding (two cases). No case was converted to radical nephrectomy. Median hospital stay was 4 d (IQR: 3–5), and the median VAS at discharge was 1 (range: 0–2). Most renal masses were malignant (79%). A positive surgical margin was found in eight cases (4.2%). Three deaths occurred, with one related to metastatic disease.

Table 3 – Surgical techniques and outcomes

Category	LESS-PN
Operative time, min	170 (130–209)
EBL, ml	150 (80–300)
Clamping, *n* (%)	
No	70 (36.8)
Yes	120 (63.2)
WIT, min	16.5 (0–26)
Additional port, *n* (%)	
No	73 (38.4)
Yes (one additional port)	117 (61.6)
Tumor resection technique, *n* (%)	
Cold scissors	152 (80)
Harmonic scalpel	12 (6.32)
Monopolar excision	14 (7.37)
Bipolar excision	12 (6.32)
Surgical approach, *n* (%)	
Transperitoneal	186 (97.9)
Retroperitoneal	4 (2.1)
Type of surgery, *n* (%)	
C-LESS	119 (62.6)
R-LESS	71 (37.4)
Access site of device, *n* (%)	
Umbilical	79 (41.58)
Pararectal	106 (55.79)
12th rib	5 (2.63)
Conversion to laparoscopy, *n* (%)	11 (5.8)
Conversion to open surgery, *n* (%)	4 (2.1)
Hospital stay, d	4 (3–5)
VAS at discharge	1 (0–2)
Length of skin incision, cm	4 (3.5–4)
Positive surgical margins, *n* (%)	8 (4.2)
Tumor recurrence, *n* (%)	2 (1)

C-LESS = conventional laparoendoscopic single-site surgery; EBL = estimated blood loss; LESS-PN = laparoendoscopic single-site partial nephrectomy; R-LESS = robotic laparoendoscopic single-site surgery; VAS = visual analog score; WIT = warm ischemia time.
Values expressed as median (interquartile range) unless otherwise specified.

3.3. *Renal functional outcomes*

A significant decrease of eGFR was observed postoperatively (postoperative vs preoperative median eGFR: 74.69 [IQR: 62.83–87.65] and 85.39 [IQR: 72.95–96.99]; $p = 0.002$) and at 6 mo (6 mo vs preoperative eGFR: 79.96 [IQR: 67.37–97.34] and 85.39 [IQR: 72.95–96.99]; $p = 0.0002$). Parallel to this, a significant increase in patients with CKD stages 3–4 (11.58% preoperatively vs 20.53% postoperatively [$p = 0.002$]; 11.58% preoperatively vs 17.37% at 6 mo [$p = 0.023$]) was found. No patient was upstaged to CKD stage 5.

3.4. *Predictors of short warm ischemia time*

Predictors of short WIT are shown in Table 4. A WIT <20 min was reported in 45 of 120 clamped cases (37.5%). ASA score and PADUA score were the only two factors significantly predicting low WIT on univariate analysis, whereas on multivariate analysis, PADUA score was the only predicting factor (low vs high score: OR: 5.11 [95% CI, 1.50–17.41]; $p = 0.009$; intermediate vs high score: OR: 5.13 [95% CI, 1.56–16.88]; $p = 0.007$).

3.5. *Predictors of non-occurrence of postoperative complications of any grade*

Table 5 shows predictors of non-occurrence of postoperative complications of any grade. Twenty-eight postoperative complications were recorded—16 early, 5 intermediate, and 1 late—for an overall complication rate of 14.7% (Clavien 1–2: 18 [64.3%]; Clavien 3–4: 10 [35.7%]). On univariate analysis, the factors associated with positive events of no postoperative complications were lower (<1)

Table 4 – Univariate and multivariate analysis of factors predicting warm ischemia time <20 minutes

Variable	Category	WIT ≤20 min		Crude	Stepwise logistic regression
		Yes	No	OR (95% CI); *p* value	OR (95% CI) *p* value
Overall, *n* (%)	–	45 (37.5)	75 (62.5)	–	–
Age, yr	≤55	27 (38.03)	44 (61.97)	1.06 (0.50–2.24); $p = 0.885$	–
	>55	18 (36.73)	31 (63.27)	1	–
Gender	Male	23 (34.85)	43 (65.15)	1	–
	Female	22 (40.74)	32 (59.26)	1.29 (0.61–2.70); $p = 0.507$	–
ASA	1	29 (42.03)	40 (57.97)	**9.42 (1.17–76.14); $p = 0.035$**	–
	2	15 (40.54)	22 (59.46)	**8.86 (1.05–75.12); $p = 0.045$**	–
	3	1 (7.14)	13 (92.86)	1	–
BMI, kg/m^2	≤26	30 (41.10)	43 (58.90)	1.49 (0.69–3.22); $p = 0.311$	–
	>26	15 (31.91)	32 (68.09)	1	–
Previous surgery	No	32 (37.65)	53 (62.35)	1.02 (0.45–2.31); $p = 0.958$	–
	Yes	13 (37.14)	22 (62.86)	1	–
PADUA score	Low (6–7)	18 (45.00)	22 (55.00)	**5.11 (1.50–17.41); $p = 0.009$**	**5.11 (1.50–17.41); $p = 0.009$**
	Intermediate (8–9)	23 (45.10)	28 (54.90)	**5.13 (1.56–16.88); $p = 0.007$**	**5.13 (1.56–16.88); $p = 0.007$**
	High (≥10)	4 (13.79)	25 (86.21)	1	1
Tumor side	Left	20 (37.74)	33 (62.26)	1.02 (0.48–2.14); $p = 962$	–
	Right	25 (37.31)	42 (62.69)	1	–
Tumor face location	Anterior	30 (35.71)	54 (64.29)	1	–
	Posterior	15 (41.67)	21 (58.33)	1.29 (0.58–2.86); $p = 0.537$	–
LESS technique	Conventional	20 (37.04)	34 (62.96)	1.04 (0.49–2.18); $p = 0.924$	–
	Robotic	25 (37.88)	41 (62.12)	1	–

ASA = American Society of Anesthesiologists; BMI = body mass index; CI = confidence interval; LESS = laparoendoscopic single-site surgery; OR = odds ratio; WIT = warm ischemia time.

Table 5 – Univariate and multivariate analysis of factors predicting non-occurrence of postoperative complication of any grade

Variable	Category	Postoperative complication		Crude	Stepwise logistic regression
		No	Yes	OR (95% CI); *p* value	OR (95% CI); *p* value
Overall	–	168 (88.42)	22 (11.58)	–	–
Age, yr	≤55	93 (91.18)	9 (8.82)	1.79 (0.73–4.42); *p* = 0.205	–
	>55	75 (85.23)	13 (14.77)	1	–
Gender	Male	95 (87.16)	14 (12.84)	1	–
	Female	73 (90.12)	8 (9.88)	1.35 (0.54–3.38); *p* = 0.528	–
ASA score	1	80 (95.24)	4 (4.76)	**4.55 (1.12–18.38); *p* = 0.033**	–
	2	66 (83.54)	13 (16.46)	1.15 (0.37–3.60); *p* = 0.805	–
	3	22 (81.48)	5 (18.52)	**1**	–
BMI, kg/m^2	≤26	91 (90.10)	10 (9.90)	1.42 (0.58–3.46); *p* = 0.442	–
	>26	77 (86.52)	12 (13.48)	1	–
Previous surgery	No	129 (89.58)	15 (10.42)	1.54 (0.59–4.06); *p* = 0.378	–
	Yes	39 (84.78)	7 (15.22)	1	–
PADUA score	Low (6–7)	83 (88.30)	11 (11.70)	0.73 (0.19–2.79); *p* = 0.646	–
	Intermediate (8–9)	54 (87.10)	8 (12.90)	0.65 (0.16–2.65); *p* = 0.551	–
	High (≥10)	31 (91.18)	3 (8.82)	1	–
Tumor size, cm	<4	138 (87.34)	20 (12.66)	1	–
	≥4	30 (93.75)	2 (6.25)	2.17 (0.48–9.80); *p* = 0.312	–
Tumor side	Left	78 (87.64)	11 (12.36)	1	–
	Right	90 (89.11)	11 (10.89)	1.15 (0.47–2.81); *p* = 0.752	–
Tumor polar location	Superior/inferior location	99 (86.09)	16 (13.91)	1	–
	Middle	69 (92.00)	6 (8.00)	1.86 (0.69–4.99); *p* = 0.218	–
Tumor rim location	Lateral	120 (86.96)	18 (13.04)	1	–
	Medial	48 (92.31)	4 (7.69)	1.80 (0.58–5.59); *p* = 0.309	–
Tumor exophytic rate, %	>50	105 (88.24)	14 (11.76)	1	–
	<50	63 (88.73)	8 (11.27)	1.05 (0.42–2.64); *p* = 0.917	–
Sinus involvement	No	129 (88.97)	16 (11.03)	1.24 (0.45–3.39); *p* = 0.674	–
	Yes	39 (86.67)	6 (13.33)	1	–
UCS involvement	No	101 (88.60)	13 (11.40)	1.04 (0.42–2.58); *p* = 0.926	–
	Yes	67 (88.16)	9 (11.84)	1	–
Tumor face location	Anterior	114 (87.02)	17 (12.98)	1	–
	Posterior	54 (91.53)	5 (8.47)	1.61 (0.56–4.60); *p* = 0.373	–
LESS technique	Conventional	98 (82.35)	21 (17.65)	**1**	**1**
	Robotic	70 (98.59)	1 (1.41)	**15 (1.97–114.14); *p* = 0.008**	**20.92 (2.66–164.64); *p* = 0.003**
Hilar clamping	No	62 (88.57)	8 (11.43)	1.02 (0.41–2.58); *p* = 0.960	–
	Yes	106 (88.33)	14 (11.67)	1	–
Intraoperative complication	No	162 (89.50)	19 (10.50)	4.26 (0.99–18.45); *p* = 0.052	–
	Yes	6 (66.67)	3 (33.33)	1	–
EBL, ml	≤250	122 (91.04)	12 (8.96)	2.21 (0.89–5.46); *p* = 0.085	**3.60 (1.35–9.56); *p* = 0.010**
	>250	46 (82.14)	10 (17.86)	1	1
OR time, min	≤180	100 (88.50)	13 (11.50)	1.02 (0.41–2.51); *p* = 0.968	–
	>180	68 (88.31)	9 (11.69)	1	–

ASA = American Society of Anesthesiologists; BMI = body mass index; CI = confidence interval; EBL = estimated blood loss; LESS = laparoendoscopic single-site surgery; OR = odds ratio; UCS = urinary collecting system.

ASA score and use of robotic LESS technique (compared with conventional LESS technique). On multivariable analyses, R-LESS (OR: 20.92 [95% CI, 2.66–164.64]; $p = 0.003$) and EBL ≤250 ml (OR: 3.60 [95% CI, 1.35–9.56]; $p = 0.010$) turned out to be independent predictors of positive events (no postoperative complications).

3.6. *Predictors of favorable outcome*

A favorable outcome was obtained in 83 cases (43.68%) (Table 6). On multivariate analysis, the only predictive factor was the PADUA score (low vs high score: OR: 4.99 [95% CI, 1.98–12.59]; $p < 0.001$; intermediate vs high score: OR: 2.28 [95% CI, 0.86–6.05], $p = 0.099$).

4. Discussion

Over the last 5 yr, LESS techniques in urology have been popularized worldwide. In a recent literature review, it was reported that the outcomes after single-site surgery in non-high-risk patients seem comparable to those of conventional laparoscopy [4]. It has been observed that LESS nephrectomy procedures, specifically, can offer a safe and efficient alternative to laparoscopy with less pain, shorter recovery time, and better cosmetic outcome. However, given the inherent limitations of the reported studies, well-designed RCTs are largely awaited to confirm and update these findings [12]. Notably, LESS has been mostly reported in the urologic literature for well-selected

Table 6 – Univariate and multivariate analysis of factors predicting a favorable outcome

Variable	Category	Positive event		Crude	Stepwise logistic regression
		No	Yes	OR (95% CI); *p* value	OR (95% CI); *p* value
Overall	–	107 (56.32)	83 (43.68)	–	–
Age, yr	≤55	58 (56.86)	44 (43.14)	1	–
	>55	49 (55.68)	39 (44.32)	1.05 (0.59–1.86); *p* = 0.87	–
Gender	Male	61 (55.96)	48 (44.04)	1.03 (0.58–1.85); *p* = 0.909	–
	Female	46 (56.79)	35 (43.21)	1	–
ASA score	1	46 (54.76)	38 (45.24)	1.96 (0.77–4.98); *p* = 0.156	–
	2	42 (53.16)	37 (46.84)	2.09 (0.82–5.34); *p* = 0.122	–
	3	19 (70.37)	8 (29.63)	1	–
BMI, kg/m^2	≤26	57 (56.44)	44 (43.56)	1	–
	>26	50 (56.18)	39 (43.82)	1.01 (0.57–1.80); *p* = 0.971	–
Previous surgery	No	78 (54.17)	66 (45.83)	1.44 (0.73–2.86); *p* = 0.291	–
	Yes	29 (63.04)	17 (36.96)	1	–
LESS technique	Conventional	61 (51.26)	58 (48.74)	1.75 (0.96–3.21); *p* = 0.070	–
	Robotic	46 (64.79)	25 (35.21)	1	–
PADUA score	Low (6–7)	41 (43.62)	53 (56.38)	**4.99 (1.98–12.59); *p* ≤ 0.001**	**4.99 (1.98–12.59); *p* ≤ 0.001**
	Intermediate (8–9)	39 (62.90)	23 (37.10)	2.28 (0.86–6.05); *p* = 0.099	2.28 (0.86–6.05); *p* = 0.099
	High (≥10)	27 (79.41)	7 (20.59)	1	1
Tumor size, cm	<4	85 (53.80)	73 (46.20)	1.89 (0.84–4.25); *p* = 0.123	–
	≥4	22 (68.75)	10 (31.25)	1	–
Tumor side	Left	51 (57.30)	38 (42.70)	1	–
	Right	56 (55.45)	45 (44.55)	1.08 (0.61–1.92); *p* = 0.796	–
Tumor polar location	Superior/inferior	57 (49.57)	58 (50.43)	**2.04 (1.11–3.72); *p* = 0.021**	–
	Middle	50 (66.67)	25 (33.33)	1	–
Tumor rim location	Lateral	70 (50.72)	68 (49.28)	**2.40 (1.21–4.76); *p* = 0.012**	–
	Medial	37 (71.15)	15 (28.85)	1	–
Tumor exophytic rate, %	>50	64 (53.78)	55 (46.22)	1.32 (0.73–2.40); *p* = 0.362	–
	<50	43 (60.56)	28 (39.44)	1	–
Sinus involvement	No	72 (49.66)	73 (50.34)	**3.55 (1.64–7.70); *p* = 0.001**	–
	Yes	35 (77.78)	10 (22.22)	1	–
UCs involvement	No	53 (46.49)	61 (53.51)	**2.83 (1.52–5.24); *p* = 0.001**	–
	Yes	54 (71.05)	22 (28.95)	1	–
Tumor face location	Anterior	74 (56.49)	57 (43.51)	1	–
	Posterior	33 (55.93)	26 (44.07)	1.02 (0.55–1.90); *p* = 0.9429	–

ASA = American Society of Anesthesiologists; BMI = body mass index; CI = confidence interval; LESS = laparoendoscopic single-site surgery; OR = odds ratio; UCS = urinary collecting system.
Favorable outcome is defined as the combined occurrence of the following events: WIT ≤20 min plus no perioperative complications plus negative surgical margins plus no conversion to open surgery or standard laparoscopy.

patients [13,14], even though experience with LESS in high-risk populations such as transplant patients has also been described [15].

The updated recommendations from the Endourological Society NOTES and LESS Working Group and the European Society of Urotechnology NOTES and LESS Working Group have noted that LESS is suitable in appropriately selected patients, including thinner patients with limited prior abdominal surgery [16].

Several series have suggested the feasibility of LESS for the management of renal malignancies [17–19]. However, whether LESS stands as a minimally invasive treatment for renal tumors remains under scrutiny [20]. At this time it seems unlikely that there will be any difference in terms of cancer control between LESS and conventional laparoscopic techniques. In a recent study, Rais-Bahrami and colleagues reported excellent short-term oncologic and renal functional outcomes for LESS-PN [21]. Nevertheless, studies with longer follow-up are awaited to address the oncologic efficacy and safety of LESS. Meanwhile, careful patient selection should be made when using LESS for upper urinary tract malignancies to optimize outcomes [13].

LESS-PN has been reported thus far by only a few groups [6–8,17,21–23]. Aron et al. initially reported five selected cases (BMI <30, tumor size <7 cm, anterior exophytic tumors with interpolar or lower pole location, and no prior abdominal surgery) [6]. In all cases, an additional trocar was used to assist in suture closure of the renal defect. Median WIT was 20 min, and one patient had postoperative bleeding and pulmonary embolism. A limitation of this study was the lack of available complete data on renal function. In pioneering the experience, Kaouk and Goel described the outcomes in seven patients undergoing single-port PN, including two robotic cases. The authors concluded that the procedure was feasible for selected exophytic tumors and speculated that robotics may improve surgical capabilities during single-port surgery [7]. More recently, this has been also suggested by Han et al., who described their experience with 14 robot-assisted LESS-PN procedures using a homemade port system. These authors concluded that the application of robot assistance

provided access for meticulous suturing of the renal parenchyma [22].

The present study represents the first large multi-institutional analysis specifically evaluating risk factors for outcomes of LESS-PN.

A technically modifiable risk factor during NSS that affects the remnant renal function is the duration of renal ischemia. The best cut-off to consider for a safe NSS procedure has been debated over the years, and it has been recently suggested to be 20 min [24]. In general, the concept that every minute of ischemia may count is recognized [25]. In contrast, the concept that the percent of parenchyma preserved rather than the actual WIT may ultimately affect the postoperative renal function has been introduced [26]. In our study, the multivariable analysis demonstrated PADUA score as the only factor significantly predicting short WIT. However, no assessment of residual renal parenchyma was performed.

Similar to what has been done for laparoscopy, LESS must be scrutinized for risk of complications. Generally, the potential for complications should be appropriately low for LESS to be offered as a reasonable alternative to more established techniques [27,28]. To date, limited data have been reported that specifically analyze the occurrence of complications during LESS. In a previous study, we analyzed the incidence of and risk factors for complications and conversions in a large contemporary series of patients treated with urologic LESS [28]. Included in the analysis were 1163 cases. A total of 120 postoperative complications occurred in 109 patients (9.4%), with major complications in only 2.4% of the entire cohort. Reconstructive procedure ($p = 0.03$), high difficulty score ($p = 0.002$), and extended operative time ($p = 0.02$) predicted high-grade complications.

According to our results, robotic surgery was more effective than C-LESS in reducing the risk for surgical complications. It can be speculated that this might be related to the facilitation of dissection and suturing during NSS.

Different access sites for LESS have been described in the literature [5,7–9,13–23]. Umbilicus intuitively represents the most attractive one, as it already represents a natural scar, although it can be more challenging, especially with specific tumor locations (eg, upper pole and/or posterior ones). It is outside the scope of this study to compare LESS access sites. But it is interesting from a technical standpoint to get an idea of how different surgeons approaching the same challenging procedure have chosen different strategies.

Notably, the use of one additional trocar was applied in 61.6% of cases in the present series, and one might argue that this represents a major bias. We embrace the concept that patient safety comes first (“do not harm”). According to current terminology [4,27], the use of an extra 3-mm trocar is still considered LESS; when more than one additional trocar is used, it is considered a conversion to standard laparoscopy. In the multi-institutional study that we recently co-authored [5], use of an additional port occurred in 23% of cases, with an overall conversion rate of 20.8%. Nevertheless, the use of an additional trocar in LESS-PN could facilitate the procedure, reduce the risk for complication, and allow for precise resection of the tumor.

The use of a combined outcome parameter has been proposed recently in the field of NSS [29]. In the present analysis, we set up an arbitrary composed parameter (ie favorable outcome) including the combination of a short (<20 min) WIT, no perioperative complications, negative surgical margins, and no conversion. Despite its novel and arbitrary definition, this parameter can be regarded as a mark of success for the given LESS-PN procedure. Not surprisingly, the PADUA score was found to be predictive of a favorable outcome, confirming findings with other minimally invasive NSS techniques [30].

When specifically assessing renal functional outcomes, a decline in eGFR and a higher rate of patients with CKD stage >2 were noted. However, a partial recovery of renal function was observed at the last available assessment at 6 mo. The observed decrease in eGFR and CKD upstaging are similar to those reported for other PN techniques [31]. To note, none of the cases required conversion to radical nephrectomy. This accounts for the surgeons’ compliance with an NSS approach, as demonstrated by the liberal use of additional ports when deemed necessary to safely complete the procedure [13,28].

This study has a few important limitations. Participating institutions were asked, and agreed, to provide their raw data to a principal investigator who collected them in a purpose-built datasheet. Even if data had been prospectively collected, biases related to the retrospective design remain true. Moreover, a centralized review of computed tomography images to score the tumors according to the PADUA system was not performed, and this can be arguably regarded as an additional bias. Moreover, these data reflect results from different surgeons, all of them sharing significant experience with laparoscopy. In addition, patient selection criteria were not standardized, surgical expertise was not quantified, and different surgical techniques were applied. Ultimately, the reported figures over time do not reflect the learning curve of a single individual. Finally, one might argue that any new surgical technique should be compared with the standard one before one can draw any conclusions concerning its benefits. In this analysis, no control group was considered because this was actually outside the scope of the present manuscript. Thus the actual benefits of LESS compared to standard laparoscopy remain to be proven. Mid- and long-term oncologic outcomes are also needed to demonstrate the oncologic equivalence of LESS-PN to open surgery or even standard laparoscopy.

5. Conclusions

Findings from the present large multicenter analysis confirm that LESS-PN represents a challenging procedure that can be safely and effectively performed by experienced hands, given a high likelihood of a single additional port. Anatomic tumor characteristics as determined by the PADUA score are independent predictors of a favorable surgical outcome. Thus patients presenting tumors with

low PADUA scores represent the best candidates for LESS-PN. Moreover, the application of a robotic platform is likely to reduce the overall risk of postoperative complications.

Author contributions: Francesco Greco had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Greco, Autorino.
Acquisition of data: Greco, Autorino, Rha, Derweesh, Cindolo, Richstone, Herrmann, Liatsikos, Sun, Nagele, Stolzenburg, Rais-Bahrami, Liss, Schips, Kassab, Wang, Kallidonis, Wu, Young, Mohammed, Haber, Springer.
Analysis and interpretation of data: Greco, Autorino.
Drafting of the manuscript: Greco, Autorino.
Critical revision of the manuscript for important intellectual content: Greco, Autorino, Rha, Derweesh, Cindolo, Richstone, Herrmann, Liatsikos, Sun, Nagele, Stolzenburg, Rais-Bahrami, Liss, Schips, Kassab, Wang, Kallidonis, Wu, Young, Springer, Fornara, Kaouk.
Statistical analysis: Fanizza.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: Fornara, Kaouk.
Other (specify): None.

Financial disclosures: Francesco Greco certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

References

[1] MacLennan S, Imamura M, Lapitan MC, et al. Systematic review of oncological outcomes following surgical management of localised renal cancer. Eur Urol 2012;61:972–93.
[2] Ljungberg B, Cowan NC, Hanbury DC, et al. EAU guidelines on renal cell carcinoma: the 2010 update. Eur Urol 2010;58: 398–406.
[3] Aboumarzouk OM, Stein RJ, Eyraud R, et al. Robotic versus laparoscopic partial nephrectomy: a systematic review and meta-analysis. Eur Urol 2012;62:1023–33.
[4] Autorino R, Cadeddu JA, Desai MM, et al. Laparoendoscopic single-site and natural orifice transluminal endoscopic surgery in urology: a critical analysis of the literature. Eur Urol 2011; 59:26–45.
[5] Kaouk JH, Autorino R, Kim FJ, et al. Laparoendoscopic single-site surgery in urology: worldwide multi-institutional analysis of 1076 cases. Eur Urol 2011;60:998–1005.
[6] Aron M, Canes D, Desai MM, Haber GP, Kaouk JH, Gill IS. Transumbilical single-port laparoscopic partial nephrectomy. BJU Int 2009;103:516–21.
[7] Kaouk JH, Goel RK. Single-port laparoscopic and robotic partial nephrectomy. Eur Urol 2009;55:1163–70.
[8] Cindolo L, Greco F, Fornara P, Mirone V, Schips L. Nephron sparing LESS: technique and review of the current literature. Arch Esp Urol 2012;65:303–10.
[9] Kaouk JH, Autorino R. Laparoendoscopic single-site surgery (LESS) and nephrectomy: current evidence and future perspectives. Eur Urol 2012;62:613–5.
[10] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
[11] Ficarra V, Novara G, Secco S, et al. Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification of renal tumours in patients who are candidates for nephron-sparing surgery. Eur Urol 2009;56:786–93.
[12] Fan X, Lin T, Xu K, et al. Laparoendoscopic single-site nephrectomy compared with conventional laparoscopic nephrectomy: a systematic review and meta-analysis of comparative studies. Eur Urol 2012;62:601–12.
[13] Greco F, Cindolo L, Autorino R, et al. Laparoendoscopic single-site upper urinary tract surgery: standardized assessment of postoperative complications and analysis of risk factors. Eur Urol 2012; 61:510–6.
[14] Raman JD, Bagrodia A, Cadeddu JA. Single-incision, umbilical laparoscopic versus conventional laparoscopic nephrectomy: a comparison of perioperative outcomes and short-term measures of convalescence. Eur Urol 2009;55:1198–206.
[15] Greco F, Wagner S, Hoda MR, Weigand K, Inferrera A, Fornara P. Single-portal access laparoscopic radical nephrectomy for renal cell carcinoma in transplant patients: the first experience. Eur Urol 2011;59:1060–4.
[16] Gettman M, White WM, Aron M, et al. Where do we really stand with LESS and NOTES? Eur Urol 2011;59:231–4.
[17] Cindolo L, Berardinelli F, Bellocci R, Schips L. Laparoendoscopic single-site unclamped nephron-sparing surgery: a case report. Eur Urol 2011;60:591–4.
[18] Greco F, Veneziano D, Wagner S, et al. Laparoendoscopic single-site radical nephrectomy for renal cancer: technique and surgical outcome. Eur Urol 2012;62:168–74.
[19] White MA, Autorino R, Spana G, et al. Robotic laparoendoscopic single-site radical nephrectomy: surgical technique and comparative outcomes. Eur Urol 2011;59:815–22.
[20] Khanna R, Laydner HK, Isac W, Stein RJ. Laparoendoscopic single-site surgery for renal malignancies. Expert Rev Anticancer Ther 2010;10:1861–3.
[21] Rais-Bahrami S, George AK, Montag S, Okhunov Z, Richstone L. Laparoendoscopic single-site (LESS) partial nephrectomy short-term outcomes. BJU Int 2013;111:264–70.
[22] Han WK, Kim DS, Jeon HG, et al. Robot-assisted laparoendoscopic single-site surgery: partial nephrectomy for renal malignancy. Urology 2011;77:612–6.
[23] Springer C, Veneziano D, Wimpissinger F, Inferrera A, Fornara P, Greco F. Clampless laparoendoscopic single-site partial nephrectomy for renal cancer with low PADUA score: technique and surgical outcomes. BJU Int. In press.
[24] Becker F, Van Poppel H, Hakenberg OW, et al. Assessing the impact of ischaemia time during partial nephrectomy. Eur Urol 2009; 56:625–35.
[25] Thompson RH, Lane BR, Lohse CM, et al. Every minute counts when the renal hilum is clamped during partial nephrectomy. Eur Urol 2010;58:340–5.
[26] Lane BR, Gill IS, Fergany AF, Larson BT, Campbell SC. Limited warm ischemia during elective partial nephrectomy has only a marginal impact on renal functional outcomes. J Urol 2011;185: 1598–603.
[27] Gill IS, Advincula AP, Aron M, et al. Consensus statement of the consortium for laparoendoscopic single-site surgery. Surg Endosc 2010;24:762–8.
[28] Autorino R, Kaouk JH, Yakoubi R, et al. Urological laparoendoscopic single site surgery: multi-institutional analysis of risk factors for conversion and postoperative complications. J Urol 2012;187: 1989–94.

[29] Khalifeh A, Autorino R, Hillyer SP, et al. Comparative outcomes and assessment of "trifecta" in 500 robotic and laparoscopic partial nephrectomies: a single surgeon experience. J Urol. In press. http://dx.doi.org/10.1016/j.juro.2012.10.021.

[30] Ficarra V, Bhayani S, Porter J, et al. Predictors of warm ischemia time and perioperative complications in a multicenter, international series of robot-assisted partial nephrectomy. Eur Urol 2012;61:395–402.

[31] Clark MA, Shikanov S, Raman JD, et al. Chronic kidney disease before and after partial nephrectomy. J Urol 2011;185:43–8.