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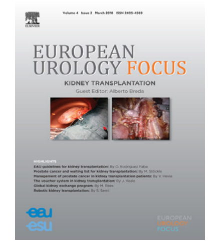

Surgery in Motion

Surgical Management of Synchronous, Bilateral Renal Masses: A 1-decade Referral Center Experience

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Abstract

Background: Management and decision-making in patients with bilateral renal masses are controversial.

Objective: To report our experience of surgical management in patients with bilateral renal masses undergoing surgery at a high-volume center.

Design, setting, and participants: We retrospectively collected data from patients treated with partial nephrectomy (PN) or radical nephrectomy for bilateral renal masses at a single referral institution between June 2008 and June 2019. Patient- and tumor-related features, timing (one vs two stage), and surgical approach (open vs robotic) were analyzed.

Surgical procedure: A one- versus two-stage strategy was adopted according to the opportunity to perform at least one PN using a clampless or selective-clamping approach, in order to avoid acute kidney injury.

Measurements: Operative time, warm ischemia time, and intra- and postoperative complications were recorded. Histopathological results and tumor histology were assessed.

Results and limitations: Overall, 41 patients were included. The median age was 67 yr and the median preoperative estimated glomerular filtration rate (eGFR) was 84 ml/min/1.73 m^2. The median Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) score was 8 (interquartile range [IQR] 7–8) for both sides. In 17 (42%) patients, a simultaneous approach was chosen, with a pure robotic approach in 11/17 cases, while among the 24 (58.6%) patients treated with a two-stage strategy, 15 (62.5%) were treated with a robotic approach on both sides. Intraoperative complications and postoperative major (CDC $\geq$3) complications were recorded in 7.3% and 4.9% of cases, respectively. The overall positive surgical margins rate was 2.4%. At a median follow-up of 42 (IQR 18–59) mo, the median eGFR was 73 (IQR 64–80) ml/min/1.73 m^2, while disease-free survival and cancer-specific mortality were 90.2% and 7.3%, respectively.

Conclusions: Our experience underlines that both simultaneous and staged surgical treatment of patients with bilateral renal masses are feasible and safe if grounded on proper patient selection.

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Patient summary: Management of patients with bilateral renal masses is challenging, given the heterogeneity of clinical scenarios and the need to optimize the timing of treatment to achieve maximal functional preservation while ensuring oncological efficacy.

1. Introduction

Bilateral, synchronous renal masses represent a challenging scenario, with an estimated incidence ranging from 1.8% up to 11% [1–5]. Management and decision-making in patients with bilateral renal masses are controversial and no formal recommendations are provided by current international guidelines on the timing of treatment, although nephron-sparing surgery (NSS) should be pursued whenever technically feasible to improve renal function preservation and lower cardiovascular morbidity [6] and all-cause mortality [7,8].

Undeniably, the demanding task to balance oncological outcomes, perioperative risk, as well as renal function preservation represents a primary goal of kidney surgery. In this scenario, several factors play a key role in determining the most appropriate strategy, including surgeon's expertise and skills, volume center, tumor size and complexity, as well as patient's comorbidity burden and preferences. Nevertheless, a clear and unanimous consensus on the ideal management of synchronous bilateral renal masses is not yet reported, and limited data are currently available [9–12]. In particular, a lot of questions are still open (ie, whether to perform preoperative renal biopsy or not, whether to proceed with a simultaneous or staged strategy or adopt uni- or bilateral pedicle clamping, and, at last, which tumor needs to be treated first).

To address this unmet need, we analyzed the prospectively collected data of consecutive patients diagnosed with synchronous, bilateral renal masses at a single high-volume center. The main endpoints of the study were the following: (1) to explore intra- and postoperative results of our series and to report the criteria followed at our center on the basis of which the ideal surgical strategy is chosen, and (2) to optimize surgical management of bilateral renal masses by proposing a flowchart that may act as the very first step toward an ideal shared treatment strategy.

2. Patients and methods

2.1. Patients, dataset, and selection

Data from 41 consecutive patients diagnosed with synchronous, bilateral renal masses between June 2008 and June 2019 were retrospectively reviewed. Preoperative features of patients including age, gender, body mass index, and comorbidity status, as assessed by the Charlson Comorbidity Index, the Eastern Cooperative Oncology Group (ECOG) performance status score, and the American Society of Anesthesiologists physical status (PS) classification system, were collected. Chest and abdominal computed tomography scan or abdomen magnetic resonance imaging with contrast enhancement were performed for preoperative staging. All patients were scored according to the Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) nephrometric classification [13]. Metastatic renal cell carcinomas (RCCs) were excluded from this study. Operative time, warm ischemia time (WIT), and intra- and postoperative complications were recorded. The severity of intra- and postoperative complications was graded according to the modified Satava [14] and the Clavien-Dindo classification system [15], respectively.

Intraoperative complications were defined as all the events occurring between the induction of anesthesia and patient awakening that could potentially cause injury and require unplanned surgical maneuvers. Postoperative complications were defined as any event occurring until the 90th postoperative day, altering the normal postoperative course and/or delaying discharge. Histopathological results and concordance of tumor histology between the two sides were assessed. Local recurrence (LR) was defined as any recurrence localized in the ipsilateral kidney (defining in each case whether distant or not from the tumor enucleation bed). Systemic recurrence (SR) was defined as any other recurrence including retroperitoneal lymph nodes or distant organs.

2.2. Surgical strategy and management

In all cases, regardless of surgical timing, partial (PN) and radical (RN) nephrectomies were performed with a robotic or an open approach based on surgeon's skills and preference. When feasible, we always prioritized a minimally invasive approach. We did not routinely perform preoperative renal biopsy according to: (1) the lack of conclusive data on accuracy of renal tumor biopsy in determining tumor histotype and grading in light of tumor heterogeneity, and (2) the possible different histological variants on both sides.

A one- versus two-stage strategy was adopted according to the opportunity to perform at least one PN using a clampless or selective-clamping approach, in order to avoid acute kidney injury (AKI). In the one-stage strategy, once the first PN had been carried out with a clampless or selective-clamping strategy, then, after patient repositioning, the PN on the contralateral side was performed with a clampless or on-clamp approach. This strategy aimed at the best renal function preservation and maximization of postoperative outcomes. Conversely, when both tumors were likely to require on-clamp PN or on-clamp PN plus RN, then a two-stage procedure was adopted. In this case, we generally started from the easier tumor first, in order to perform the second procedure for the more complex tumor (whether PN or RN), in an "elective" setting, starting from an optimal residual renal function. In a minority of cases, when one of the renal tumors presented with local symptoms, gross hematuria, or thrombus of the renal vein, we decided to treat the more complex tumor first. Figure 1 depicts a detailed decision tree flowchart, reporting the criteria adopted at our center for the management of synchronous, bilateral renal masses.

2.3. Surgical technique

A detailed illustration of the surgical technique employed at our institution can be found in the accompanying video material. We performed open and robotic approaches as reported previously by our group [16].

In brief, in case of open surgery, patients were treated with a lateral retroperitoneal approach and placed in an oblique position elevated by approximately 75°, with the incision made at above the 11th intercostal space.

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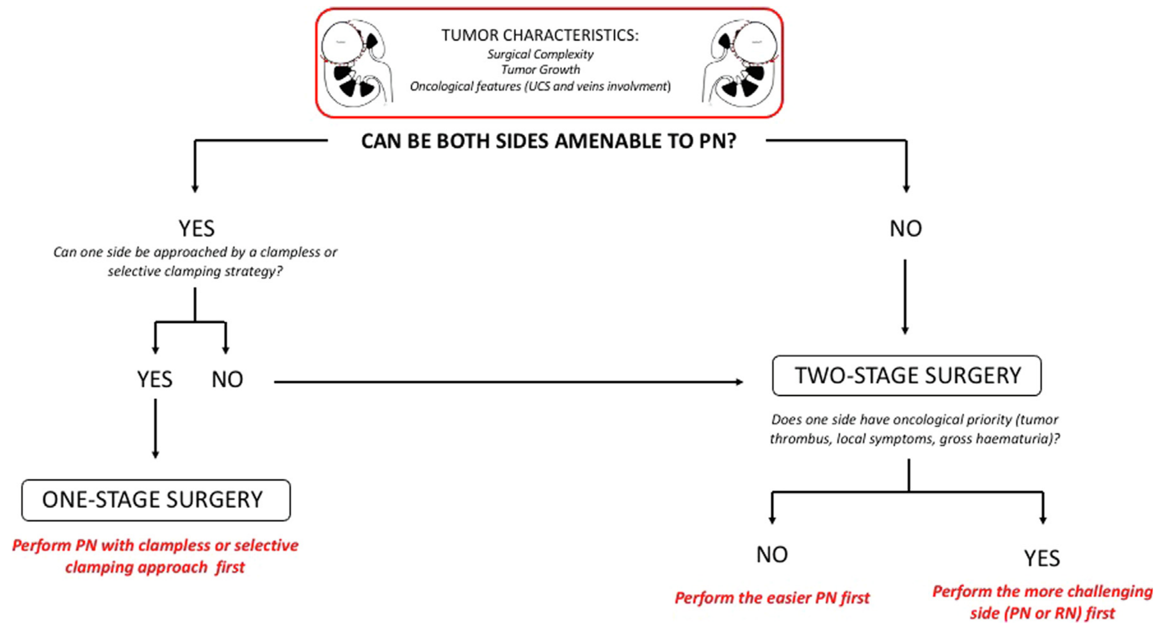

Fig. 1 – Flow diagram depicting a proposed decision-making model for surgical management of synchronous, bilateral renal masses. PN = partial nephrectomy; RN = radical nephrectomy; UCS = urinary collecting system.

Conversely, to achieve robotic PN, the Da Vinci Si system was used in all the cases (Intuitive Surgical, Sunnyvale, CA, USA), in a three-arm configuration with a 30° laparoscope. For the transperitoneal approach, the patient was positioned in the flank position, elevated at approximately 70°. One paraumbilical 12-mm trocar for the camera plus two 8-mm ports for the robotic instruments were used (one in midclavicular line 3 cm below the costal margin, and another one caudally and on the same line to obtain optimal triangulation). Two 5- and 12-mm Airseal additional ports for the assistant were inserted approximately on the same line of the camera port. In case of challenging, highly complex renal masses (ie, PADUA $\geq$10) or in case of RN, usually a four-arm configuration was preferred. Such a configuration aimed to achieve better traction during the isolation of the renal mass and the excision phase, as well as a greater exposure of tumor resection bed during renorrhaphy. In this specific case, the camera port was usually placed more cranially, about 1–2 cm laterally from the pararectal line, to have enough space caudally to insert the fourth robotic arm.

For the retroperitoneal approach, the patient was placed in flank position, elevated at approximately 90°. After the access at the level of the midiliac crest, the fingertip was used to mobilize the peritoneum and to create the retroperitoneal space. A three-arm configuration was used, including one 12-mm trocar for the camera at the level of the first incision and two 8-mm trocars for the robotic arms, with the first placed at the level of the lateral border of the peritoneal reflection and the second at the lateral border of the paraspinal muscles. A 12-mm Airseal trocar for the assistant was placed on the anterior axillary line between the camera and one of the robotic arms. One additional 5-mm port for the assistant may be placed.

Port placement in single-stage surgery may significantly vary case by case according to patient habitus and the nephrometric characteristics of both renal masses. Basically, in case of nonobese patients, it is usually possible to reuse the camera port and the incision for the 12- and 5-mm ports of the assistant whenever a transperitoneal approach is planned for both sides. Of course, this becomes a difficult task to achieve in case of obese patients (in whom the camera and the assistant ports needs to be placed more laterally), in case of highly complex renal masses (therefore, having to place the camera 3–4 cm more cranially due to the need for the fourth robotic arm caudally), or when a combined transperitoneal-retroperitoneal approach is preferred. Patient positioning follows the rules listed above. After having performed NSS for the first tumor, the robot was undocked and the patient positioned on the contralateral flank for subsequent PN.

2.4. Statistical analysis

Categorical and continuous nonparametric variables were reported as frequencies and proportions or as median and interquartile range (IQR), respectively. Pearson's chi-square test was used for dichotomous variables. Mann-Whitney U test was used to compare continuous variables. The probability of survival was assessed by the Kaplan-Meier method, with the log-rank test (Mantel-Cox) used to estimate differences among levels of the analyzed variables. Statistical significance in this study was set as $p \leq 0.05$. All reported p values are two sided. Analyses were performed with SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

3. Results

Overall, baseline features of 41 patients presenting with synchronous, bilateral renal masses are summarized in Table 1. The median age was 67 (IQR 58–73) yr and male patients accounted for 78%. The preoperative estimated glomerular filtration rate (eGFR) was 84 (IQR 75–89) ml/min/m^2, while the median tumor size was 3 cm for both sides (IQR 2–6 cm on the left and 2.2–4.2 cm on the right). None of the patients presented with multiple renal masses in one kidney.

The surgical and pathological features are reported in Table 2. Overall, a double robotic approach was performed in 26 (63.4%) patients, a combined robotic and open strategy was preferred in two (4.9%) cases, while a bilateral open approach was carried out in 13 (31.7%) cases. Thirty-seven (90.2%) patients received bilateral PN, three (7.3%) had PN plus RN, while only one (2.5%) underwent bilateral RN. No

Table 1 – Preoperative characteristics of 41 patients treated synchronous, bilateral, localized renal masses

Preoperative features		Bilateral renal masses (*n* = 41)	
Gender, *n* (%)			
	Male	32	(78)
	Female	9	(22)
Age (yr), median (IQR)		67	(58–73)
BMI (kg/m^2), median (IQR)		26.5	(24.6–28)
Charlson Comorbidity Index, median (IQR)		3	(2–4)
ASA score, median (IQR)		2	(2–3)
Preoperative eGFR, median (IQR)		84	(75–89)
Left tumor clinical size (cm), median (IQR)		3	(2–6)
Right tumor clinical size (cm), median (IQR)		3	(2.2–4.2)
PADUA left tumor, median (IQR)		8	(7–8)
PADUA right tumor, median (IQR)		8	(7–8)
Left tumor PADUA complexity, *n* (%)			
	6–7	20	(48.8)
	8–9	19	(46.3)
	≥10	2	(3.9)
Right tumor PADUA complexity, *n* (%)			
	6–7	14	(34.1)
	8–9	20	(48.8)
	≥10	7	(17.1)
RENAL left tumor, median (IQR)		7	(6–7)
RENAL right tumor, median (IQR)		7	(6–8)
Left tumor RENAL complexity, *n* (%)			
	4–6	16	(39)
	7–9	22	(53.7)
	10–12	3	(7.3)
Right tumor RENAL complexity, *n* (%)			
	4–6	12	(29.3)
	7–9	21	(51.2)
	10–12	8	(19.5)
Left tumor cT stage, *n* (%)			
	1	26	(63.4)
	2	11	(26.8)
	3	4	(9.8)
Right tumor cT stage, *n* (%)			
	1	29	(70.7)
	2	8	(19.5)
	3	3	(7.3)
	4	1	(2.4)

ASA = American Society of Anesthesiologists; BMI = body mass index; eGFR = estimated glomerular filtration rate; IQR = interquartile range; PADUA = Preoperative Aspects and Dimensions Used for an Anatomical.

conversions from robotic to open approach were recorded. We registered three (7.3%) Satava grade 1 intraoperative complications, namely, the onset of intraoperative bleeding requiring blood transfusions, while Clavien-Dindo 2 and 3 postoperative complications were recorded in three (7.3%) and two (4.9%) cases, respectively. The most prevalent histotype was clear cell RCC, recorded in 62.1% of specimens, irrespective of tumor side. The concordance of tumor histology on both sides was 81.5%. In case of tumor discordance between the two sides, the most common tumor histology association was clear cell RCC plus papillary RCC, found in four out of eight patients. Only one (2.4%) positive surgical margin was recorded. At a median follow-up of 42 (IQR 18–59) mo, the median eGFR was 73 (IQR 64–80) ml/min/m^2 and disease-free survival was equal to 90.2%. In particular, one (2.4%) patient experienced LR localized far from the tumor resection bed, while three (7.3%) patients experienced SR and cancer-specific death.

The clinical, surgical, and postoperative features of synchronous, bilateral renal masses divided according to the timing of surgery are summarized in Table 3. Overall, 17 (41.4%) and 24 (58.6%) patients were treated with a one- and a two-stage strategy, respectively. Among patients undergoing two-stage surgery, the tumor with a lower nephrometric score was treated first in 15 (62.5%) cases and the median time between the two surgical procedures was 82 (IQR 58–112) d. Patients treated with a two-stage strategy showed significantly higher median cumulative operative time (310 vs 240 min; p = 0.01), WIT (18 vs 10 min; p = 0.03), and length of stay (10 vs 6 d; p = 0.01) than patients receiving simultaneous surgery. However, no significant differences were found according to the median ΔeGFR (ml/min/1.73 m^2) among baseline and 3 mo (−9.2 [IQR −15.2; −6.6] vs −9.6 [IQR −16.1; −6.3, p = 0.41]) and last follow-up values (−7.3 [IQR −12.6; −5.6] vs −7.8 [IQR −15.4; −5.6, p = 0.31]) in patients treated with simultaneous versus staged surgery. Similarly, at survival analysis, no significant difference emerged between the two groups according to disease-free survival (82.4% vs 95.8%; p = 0.14).

4. Discussion

It is widely accepted that bilateral renal masses can represent a non-negligible challenging task. Indeed, although the presence of bilateral renal masses is one of the estab-

Table 2 – Surgical and postoperative characteristics of 41 patients treated synchronous, bilateral, localized renal masses

Surgical and pathological features		Bilateral tumor (*n* = 41)	
Type of approach, *n* (%)			
	Robotic + robotic	26	(63.4)
	Robotic + open	2	(4.9)
	Open + open	13	(31.7)
Type of surgery, *n* (%)			
	PN + PN	37	(90.2)
	PN + RN	3	(7.3)
	RN + RN	1	(2.4)
Clamping approach, *n* (%)			
	Bilateral main artery clamping	19	(46.3)
	Monolateral main artery clamping	8	(19.5)
	Bilateral selective artery clamping	3	(7.3)
	Monolateral selective artery clamping	4	(9.8)
	Bilateral clampless	3	(7.3)
	Bilateral RN	1	(2.4)
	Monolateral main artery clamping + contralateral RN	1	(2.4)
	Monolateral selective artery clamping + contralateral RN	1	(2.4)
	Clampless PN +contralateral RN	1	(2.4)
Intraoperative complications, *n* (%)			
	Absent	38	(92.7)
	Satava grade 1	3	(7.3)
Postoperative complications, *n* (%)			
	Absent	36	(87.8)
	Clavien-Dindo 2	3	(7.3)
	Clavien-Dindo 3	2	(4.9)
Histotype left tumor, *n* (%)			
	ccRCC	25	(61)
	pRCC I	4	(9.8)
	pRCC II	1	(2.4)
	cRCC	3	(7.3)
	Oncocytoma	6	(14.6)
	AML	2	(4.9)
Histotype right tumor, *n* (%)			
	ccRCC	26	(63.4)
	pRCC I	3	(7.3)
	pRCC II	1	(2.4)
	cRCC	5	(12.2)
	CDC	1	(2.4)
	Oncocytoma	3	(7.3)
	AML	2	(4.9)
Concordance of histotype between the two sides, *n* (%)		33	(81.5)
Positive surgical margins, *n* (%)		1	(2.4)
Oncological outcome, *n* (%)			
	Disease free	37	(90.2)
	Local recurrence	1	(2.4)
	Systemic recurrence	3	(7.3)
	Cancer-specific death	3	(7.3)
Months of follow-up, median (IQR)		42	(18–59)
3-mo follow-up eGFR (ml/min/1.73 m^2), median (IQR)		68	(59–78)
Last follow-up eGFR, median (IQR)		73	(64–80)

AML = angiomyolipoma; CDC = Centers for Disease Control and Prevention; cRCC = cystic renal cell carcinoma; ccRCC = clear cell renal cell carcinoma; eGFR = estimated glomerular filtration rate; IQR = interquartile range; PADUA = Preoperative Aspects and Dimensions Used for an Anatomical; PN = partial nephrectomy; pRCC = papillary renal cell carcinoma; RN = radical nephrectomy.

lished indications for NSS, the urologist should try to thoroughly balance oncological safety, perioperative risk, and functional outcomes when approaching bilateral renal masses.

In this scenario, several factors play a role in determining the optimal management strategy, including surgeon's expertise and skills, center volume, tumor nephrometry, and complexity, as well as patient's comorbidity burden and preferences. As such, there is considerable debate about the optimal approach for managing bilateral renal masses and a lot of questions are still open: (1) Is it advisable to perform renal biopsy before surgery? If yes, would you consider unilateral or bilateral renal biopsy? (2) Should the masses be treated with RN or PN? (3) What is the role for open versus minimally invasive procedures? (4) Not least, which is the optimal timing for surgery? Should we adopt a simultaneous or staged surgical strategy? In the current paper, we tried to provide an answer to the abovementioned questions by analyzing the data of consecutive patients diagnosed with synchronous, bilateral renal masses at our institution, specifically focusing on surgical, oncological, and functional outcomes. In addition, we present our contemporary algorithm for managing this particular surgical scenario.

The first key message of the current paper is that we do not perform preoperative renal biopsy routinely. Indeed, pathological assessment of renal tumors via percutaneous biopsy or fine needle aspiration is often limited by insufficient sampling, false negatives, inability to establish pathological data regarding perirenal fat, vascular invasion, and

Table 3 – Clinical, surgical, and postoperative features of 41 patients treated for synchronous, bilateral, renal masses divided according to the timing of surgery

		One-stage strategy (n = 17, 41.4%)		Two-stage strategy (n = 24, 58.6%)		p value
Gender, n (%)						
	Male	13	(76.5)	19	(79.2)	0.83
	Female	4	(23.5)	5	(20.8)	
Age (yr), median (IQR)		64	(58–77)	69	(58–73)	0.61
Charlson Comorbidity Index, median (IQR)		3	(2–3)	3	(3–5)	0.19
BMI (kg/m^2), median (IQR)		27.3	(24.5–27.8)	26.3	(24.8–28.2)	0.89
ASA score, median (IQR)		2	(2–3)	2	(2–3)	0.94
Preoperative eGFR, median (IQR)		86	(75–89)	83	(75–88)	0.55
Left tumor clinical diameter (cm), median (IQR)		2.5	(2–4.1)	3.9	(2.7–6.3)	0.13
Right tumor clinical diameter (cm), median (IQR)		2.5	(1.8–4.0)	3.3	(2.5–4.5)	0.78
PADUA left tumor, median (IQR)		7	(6–8)	8	(7–9)	0.51
PADUA right tumor, median (IQR)		8	(7–8)	8	(8–8)	0.29
Left tumor PADUA complexity, n (%)						
	6–7	11	(64.7)	9	(37.5)	0.15
	8–9	6	(35.3)	13	(54.2)	
	≥10	0	(0)	2	(8.3)	
Right tumor PADUA complexity, n (%)						
	6–7	8	(47.1)	6	(25)	0.32
	8–9	7	(41.2)	13	(54.2)	
	≥10	2	(11.8)	5	(20.8)	
RENAL left tumor, median (IQR)		6	(5–7)	7	(6–8)	0.23
RENAL right tumor, median (IQR)		7	(6–8)	8	(7–8)	0.15
Left tumor RENAL complexity, n (%)						
	4–6	9	(52.9)	7	(29.2)	0.11
	7–9	8	(47.1)	14	(58.3)	
	10–12	0	(0)	3	(12.5)	
Right tumor RENAL complexity, n (%)						
	4–6	7	(41.2)	5	(20.8)	0.27
	7–9	7	(41.2)	14	(58.3)	
	10–12	3	(17.6)	5	(20.9)	
Left tumor cT stage, n (%)						
	1	12	(70.6)	14	(58.3)	0.67
	2	4	(23.5)	7	(29.2)	
	3	1	(5.9)	3	(12.5)	
Right tumor cT stage, n (%)						
	1	13	(76.5)	16	(66.7)	0.80
	2	3	(17.6)	5	(20.8)	
	3	1	(5.9)	2	(8.3)	
	4	0	(0)	1	(4.2)	
Type of approach, n (%)						
	Robotic + robotic	11	(64.8)	15	(62.5)	0.46
	Robotic + open	0	(0)	2	(8.3)	
	Open + open	6	(35.2)	7	(29.1)	
Type of surgery, n (%)						
	PN + PN	15	(88.2)	22	(91.7)	0.47
	PN + RN	1	(5.9)	2	(8.3)	
	RN + RN	1	(5.9)	0	(0)	
Cumulative operative time (min), median (IQR)		240	(210–300)	310	(263–388)	0.01
Cumulative WIT (min), median (IQR)		10	(0–18)	18	(12–35)	0.03
Intraoperative complications, n (%)						
	Absent	16	(94.1)	22	(91.2)	0.23
	Satava grade I	1	(5.9)	2	(8.3)	
Postoperative complications, n (%)						
	Absent	14	(82.4)	22	(91.7)	0.23
	Clavien-Dindo 2 (transfusion)	1	(5.9)	2	(8.3)	
	Clavien-Dindo 3 (artery embolization)	2	(11.8)	0	(0)	
Cumulative LOS (d), median (IQR)		6	(6–7)	10	(9–11)	0.01
Positive surgical margins, n (%)		0	(0)	1	(4.2)	0.39
Histotype tumor left, n (%)						
	ccRCC	13	(76.5)	12	(50)	0.55
	pRCC I	1	(5.9)	3	(12.5)	
	pRCC II	0	–	1	(4.2)	
	chRCC	1	(5.9)	2	(8.3)	
	Oncocytoma	2	(11.8)	4	(16.7)	
	AML	/		2	(8.3)	
Histotype tumor right, n (%)						
	ccRCC	11	(64.7)	15	(62.5)	0.41
	pRCC I	2	(11.8)	1	(4.2)	
	pRCC II	0	(0)	1	(4.2)	
	chRCC	1	(5.9)	4	(16.7)	
	CDC	1	(5.9)	0	(0)	

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		One-stage strategy (n = 17, 41.4%)		Two-stage strategy (n = 24, 58.6%)		p value
	Oncocytoma	2	(11.8)	1	(4.2)	
	AML	0	(0)	2	(8.3)	
Oncological outcome, n (%)						
	Disease free	14	(82.4)	23	(95.8)	0.14
	Local recurrence	0	(0)	1	(4.2)	
	Cancer-specific death	3	(17.6)	0	(0)	
Months of follow-up, median (IQR)		46	(18–58)	37	(18–84)	0.89
3-mo follow up eGFR, median (IQR)		72	(64–80)	66	(55–76)	0.23
ΔeGFR (ml/min/1.73 m^2) baseline—3 mo		−9.2	(−15.2; −6.6)	−9.6	(−16.1; −6.3)	0.41
Last follow-up eGFR, median (IQR)		76	(68–80)	71	(61–79)	0.22
ΔeGFR (ml/min/1.73 m^2) baseline—last follow-up		−7.3	(−12.6; −5.6)	−7.8	(−15.4; −5.6)	0.31

ASA = American Society of Anesthesiologists; AML = angiomyolipoma; BMI = body mass index; CDC = Centers for Disease Control and Prevention; ccRCC = clear cell renal cell carcinoma; eGFR = estimated glomerular filtration rate; chRCC = chromophobe renal cell carcinoma; IQR = interquartile range; LOS = length of stay; PADUA = Preoperative Aspects and Dimensions Used for an Anatomical; PN = partial nephrectomy; pRCC = papillary renal cell carcinoma; RN = radical nephrectomy; WIT = warm ischemia time.

tumor grading, as well as the difficulty in differentiating between oncocytic type neoplasms [17]. Moreover, the histopathology concordance rate between the two sides in our series was 81.5%, highlighting a non-negligible risk of discordant histology and, thus, further undermining the final reliability of tumor biopsy during the decision-making process. Interestingly, in case of tumor histology discordance, the most prevalent association observed was clear cell RCC plus papillary RCC, found in 50% of patients.

The second key point of our study is that PN was always prioritized, whenever technically feasible, since it is now widely accepted that PN provides equivalent oncological outcomes to RN with a lower decline in renal function and, therefore, a consequent reduction in the risk of cardiovascular events [6] and the risk of death [18,19]. However, despite maximal effort, not all bilateral renal tumors are amenable to PN and RN might still be required, especially for larger and highly complex masses.

Similarly, whenever possible, robotic assistance was employed. The wide maneuverability of the robotic instruments and their design, together with the increased vision of the camera make robotic surgery very precise during the tumor excision phase. In particular, despite the lack of tactile feedback, in case of PN, the surgeon can perform tumor enucleation achieving accurate blunt dissection, following the natural cleavage plane between the healthy parenchyma and tumor pseudocapsule and, at the same time, keeping always in sight the tumor edges during enucleation in order to reduce the risk of violating its boundaries [16,20,21]. Moreover, through a skillful and wise reuse of several skin incisions used for trocar placement for contralateral kidney, robotic surgery allows a further reduction in the aesthetic impact of bilateral renal surgery. Only in case of large, highly complex, bilateral renal masses, an open approach was preferred, since it was likely that these tumors were not amenable to a minimally invasive approach and the advantages of robotic assistance would have probably been lost. Moreover, we would like to point out that, in our experience, cases treated with a bilateral open approach mostly referred to the beginning of the series, with robotic assistance not being available yet or being in the very early phase of robotic learning curve. The efficacy and safety of our surgical strategy are also underlined by the relatively low intra- and postoperative complication rates. One might argue that the intraoperative complication rate could appear to be slightly higher than expected. However, if we consider the total number of intraoperative complications recorded per procedure, rather than per patient, the intraoperative complication rate decreases down to 4.6%, which is in line with the current literature [22]. More interestingly, two out of three intraoperative complications recorded were associated with an open approach. Such a finding might further highlight the benefits of robot-assisted surgery. Indeed, also in the abovementioned paper by Minervini et al [22] relying on the RECORd1 project, an open approach had been confirmed as an independent predictor of intraoperative complications, as compared with a robotic approach.

As concerns the optimal timing for surgery, no absolute consensus exists regarding whether to prefer a one- or two-stage strategy. Few single- and multi-institutional series in the past tried to provide an answer [23–26]; however, these studies were burdened by non-negligible technical and selection biases, including limited sample size, long enrollment period, inclusion of metastatic RCCs, and a lack of clear indication about surgical strategy employed. More recently, Qi et al [27] reported their surgical experience with synchronous, bilateral renal tumors, highlighting how the vast majority of patients underwent bilateral surgeries in staged procedures, except for one patient who underwent simultaneous bilateral PN. Conversely, Hu et al. [28] recently opted for a simultaneous surgical strategy in case of favorable patient physical status (ECOG PS = 0), while they chose a staged approach in case of larger tumors or patients with ECOG PS >1. Moreover, they highlighted how the more difficult tumor should generally be treated first in case of a two-stage strategy, except in case of complex tumors amenable to PN on one side with the contralateral kidney likely to be treated with RN. In this particular case, the NSS procedure should be performed earlier than contralateral RN. Our management is slightly different. First, a simultaneous versus staged surgical strategy was adopted according to the opportunity to perform at least one PN with a clampless or selective-clamping approach. In case of a one-stage strategy, we usually treated the easier tumor with PN, adopting a clampless or selective-clamping approach. Soon thereafter, the PN on the contralateral side was performed with a clampless or on-clamp approach.

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We never performed one-stage bilateral surgery whenever we thought bilateral clamping would be necessary, even if a hilar clamping was required for a short period of time on one side, since in both cases, the risk of acute kidney injury may overwhelm the benefits of single-stage surgery. This particular strategy aims to achieve the best renal function preservation and maximization of perioperative outcomes. Conversely, when both tumors were likely to require on-clamp PN or on-clamp PN plus RN, then a staged procedure was adopted. In case of bilateral PN by an on-clamp approach, once again, we usually started managing the easier tumor first. Then, we performed contralateral PN or RN for the more complex tumor in an "elective" setting, after proper patient recovery. Only in few cases, we started from the most complex tumor, according to the oncological risk (ie, thrombus of the renal vein) or presence of local symptoms. In such cases, excising the more involved tumor first might mitigate the risk of metastasis, which is theoretically higher for larger renal masses with neoplastic involvement of renal vein. Most importantly, we did not find any significant difference in disease-free survival between patients treated with a one- or two-stage strategy. In addition, although patients treated with staged surgery had significantly higher cumulative WIT, this did not translate into worse functional outcomes. Indeed, tailoring and individualizing surgical strategy on each patient allowed maximization of renal function preservation, as shown by a comparable eGFR drop between the two groups at 3-mo evaluation and last follow-up. One might argue that recent evidence reported WIT length during PN having a negligible impact on the long-term renal function outcomes in patients having two kidneys and preserved preoperative renal function [29]. However, in that case, the authors explored a slightly different clinical scenario, specifically focusing on long-term renal function after unilateral on-clamp PN. We do not know what the effects of the cumulative WIT might be on kidney function, and specifically on the risk of AKI. We believe that bilateral renal clamping would simply accentuate the AKI risk without having a tangible benefit.

Finally, we do not exactly know what might be the optimal timing between the two procedures in case of staged PN. We decided to wait approximately 2–3 mo (median time nearly 80 d) to allow complete functional recovery from previous NSS before inducing a new AKI episode. This has provided excellent short- and medium-term functional outcomes without compromising cancer control. Further studies would be needed to assess whether a shorter time between the two surgeries might be safe and effective as well.

The present study is not devoid of limitations. First, no randomization was provided between patients with a one- or two-stage strategy. Moreover, the relatively small sample size, the retrospective nature of the study, and the multiple-surgeon setting might have introduced a statistical bias. Second, procedures were all performed by experienced surgeons at a single high-volume referral center; as such, our results might not be applicable to all surgeon- or center-related scenarios. Third, the wide enrolment period may have limited the significance of the outcomes examined and could not be totally contemporary. Each of these factors might have weakened the overall reliability of reported findings.

Acknowledging these limitations, the present study represents one of those with the largest recent experience so far reporting the management and perioperative outcomes of synchronous, bilateral renal masses. It is of pivotal importance that the surgical approach is carried out by surgeons with extensive experience in kidney surgery. Even in case of highly trained surgeons, undeniably experience raises case by case. Luckily, recent new tools and technologies may help the surgeon in tailoring the most appropriate surgical strategy. In this regard, the employment of three-dimensional reconstructions and augmented reality [30] can ameliorate the assessment of tumor anatomy, permitting wiser surgical planning as well as better functional preservation due to a more precise perception of vascular anatomy potentially leading to a selective or "hybrid" (selective plus total) clamping strategy. This may also contribute to expanding the indications of NSS also for highly complex masses.

Our experience underlines that both simultaneous and staged surgical treatment of patients with bilateral renal masses are feasible and safe if grounded on proper patient selection. Larger randomized series would be needed to confirm our preliminary results, also considering whether surgeon's learning curve and the employment of three-dimensional reconstructions and augmented reality might influence perioperative outcome and the choice of the surgical strategy.

5. Conclusions

Bilateral renal masses represent a challenging surgical scenario. There is still a lack of international guideline recommendations about the management of this condition. In our experience, a simultaneous or staged surgical approach was thoroughly chosen case by case in order to maximize renal function preservation and oncological outcomes.

Author contributions: Andrea Minervini 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: Minervini, Di Maida.
Acquisition of data: Grosso, Sforza, Lambertini, Nardoni.
Analysis and interpretation of data: Di Maida, Mari, Grosso.
Drafting of the manuscript: Di Maida, Sforza, Grosso.
Critical revision of the manuscript for important intellectual content: Cocci, Mari, Siena, Tuccio, Masieri.
Statistical analysis: Di Maida, Grosso, Sforza.
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Appendix A. Supplementary data

The Surgery in Motion video accompanying this article can be found in the online version at https://doi.org/10.1016/j.euf.2022.01.010 and via www.europeanurology.com.

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