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# The correlation between affected renal function and affected renal residual volume

## A retrospective outcome of laparoscopic nephron-sparing partial nephrectomy with segmental renal artery blocking-up for localized renal tumors

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**Abstract**

Laparoscopic nephron-sparing partial nephrectomy with segmental renal artery blocking (SRPN) has been widely used in the treatment of localized renal tumors. However, the impact of ischemia-reperfusion injury (IRI) during SRPN remains controversial. This study aims to evaluate the correlation between affected renal function and affected renal volume after SRPN for localized renal tumor treatment, explore the effect of IRI on renal function after SRPN.

A total of 39 patients who underwent SRPN for localized renal tumor from June 2009 to April 2012 were reviewed. These patients were followed-up for 5 years. The preoperative affected renal glomerular filtration rate ($aGFR_{pre}$), postoperative affected renal glomerular filtration rate ($aGFR_{post}$), preoperative affected renal volume ($aVol_{pre}$), and postoperative affected renal volume ($aVol_{post}$) were collected during the follow-up period. The correlation between $aGFR_{post}/aGFR_{pre}$ and $aVol_{post}/aVol_{pre}$ was compared.

A total of 33 patients were successfully followed up. After 3, 6, 12, 24, and 60 months, $aGFR_{post}$ was $34.6 \pm 4.6$, $34.7 \pm 4.8$, $34.9 \pm 4.4$, $35.1 \pm 4.4$, and $35.2 \pm 4.2$ mL/min. The correlation coefficients between $aGFR_{post}/aGFR_{pre}$ and $aVol_{post}/aVol_{pre}$ were 0.659 ($P = .000$), 0.667 ($P = .000$), 0.663 ($P = .000$), 0.629 ($P = .000$), and 0.604 ($P = .000$), respectively. The limitation of this study was the small cohort size.

For the localized renal tumor, $aGFR_{post}$ was associated with $aVol_{post}$, but was not associated with intraoperative factors, such as the time of clamping of the affected segmental renal artery. As a part of nephrons, the resected tumor tissue caused the lack of inherent nephrons, resulting in the loss of renal function. More nephrons should be maintained before resecting the tumor completely during SRPN.

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**Abbreviations:** $aGFR_{post}$ = postoperative affected GFR, $aGFR_{pre}$ = preoperative affected GFR, $aVol_{post}$ = postoperative affected renal residual volume, $aVol_{pre}$ = preoperative affected renal volume, BMI = body mass index, CT = computed tomography, DFS = disease-free survival, eGFR = estimated glomerular filtration rate, GFR = glomerular filtration rate, IRI = ischemia-reperfusion injury, LPN = laparoscopic partial nephrectomy, OS = overall survival, PN = partial nephrectomy, WIT = warm ischemic time.

**Keywords:** affected renal residual volume, ischemia-reperfusion injury, laparoscope, nephron-sparing partial nephrectomy, postoperative affected renal function, renal tumor, segmental renal artery blocking

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## 1. Introduction

Partial nephrectomy (PN) has been demonstrated to be safe and feasible for localized renal tumor. Furthermore, PN has been recommended for the treatment of localized renal cell carcinoma by the European Association of Urology in 2014,[1,2] including open partial nephrectomy, laparoscopic partial nephrectomy (LPN), and robot-assisted partial nephrectomy. Renal hilar control, including main renal arterial clamping, segmental renal arterial clamping, and selective arterial clamping, which is guided by near-infrared fluorescence imaging, without arterial clamping and targeted vascular microdissection, is crucial to ensure a clear operative area during PN, and plays a prominent role in surgery. The methods for renal hilar control have been confirmed to be safe and feasible.[3–7] Given the challenges of main renal artery clamping, other methods have emerged as novel techniques to facilitate minimally invasive surgery by blocking the delicate blood-supply of the tumor and reducing ischemia-reperfusion injury (IRI) to the residual nephron during the operation. Due to the economic burden of patients in certain places in China, the da Vinci Si Surgical System could not be implemented. LPN is a minimally invasive procedure for small renal tumors,[7–10] and laparoscopic nephron-sparing partial nephrectomy with segmental renal artery blocking (SRPN) has been the routine treatment in the Affiliated Hospital of Guizhou Medical University and the Third Central Hospital of Tianjin.

PN surgery has been widely used as a standard of care for localized small renal tumors,[2,7,11] but factors that affect postoperative renal function have been highlighted in previous researches.[12–14] Warm ischemic time (WIT) has been considered the main factor influencing postoperative renal function after PN for a long period of time,[12,15–17] and some articles[16,18,19] have concluded that IRI was the detriment of renal function after PN surgery in the early postoperative period. At the same time, Bagheri et al[20] used the estimated glomerular filtration rate (eGFR) for the 1-year follow-up, and found that postoperative renal function was independent of IRI. In contrast, renal function was associated with renal volume rather than the effects of IRI at the late time point.[19] Precise segmental clamping of the renal artery can reduce damage induced by IRI after PN.[7,17,21] Many scholars have cited various criticisms, providing various trains of thought for designing a series of studies about the impact of WIT in PN. However, they were not able to arrive at a unified conclusion.

Renal function and renal volume have a strong relationship in normal humans without any disease with regard to the kidneys.[22–24] According to a study for normal volunteers, the glomerular filtration rate (GFR) is the most direct and accurate replacement indictor of renal function.[23,25] Nevertheless, the relationship between renal function and renal volume after the treatment of PN has rarely been reported.

The conclusions of previous studies on the influence of IRI have been contradicting. Hence, results on the impact of IRI after PN surgery remain inconsistent. At the same time, most of these studies used eGFR or serum creatinine to analyze factors that influence the affected renal function after PN. However, the follow-up time was too short or <5 years. During the follow-up period, $aGFR_{post}$ decreased, compared with $aGFR_{pre}$. We designed a 5-year retrospective cohort study and explored the cause of the decline in $aGFR_{post}$ with the loss of inherent nephrons or the impact on IRI.

## 2. Methods

### 2.1. Data acquisition

Thirty-nine patients with localized renal tumors were treated by SPRN between June 2009 and April 2012 in the Affiliated Hospital of Guizhou Medical University and the Third Central Hospital of Tianjin. The present study was approved by the Ethics Committee of the Affiliated Hospital of Guizhou Medical University and the Third Central Hospital of Tianjin, and all included patients provided a signed informed consent. The inclusion criteria of the present study were as follows:

(1) patients who had an indication of PN, accepted SRPN, and was not converted to open surgery;
(2) patients with localized renal tumors, and the diameter of the tumor was not more than 4 cm;
(3) the distance between the edge of the tumor and renal pedicle should be ≥3 cm;
(4) patients with renal tumors confirmed by imaging examinations, and the stage of the tumor should not be higher than pT1a, according to the 2010 American Joint Committee on Cancer renal tumor staging criteria;
(5) preoperative renal computed tomography angiography revealed tumor blood supplied from the kidney's secondary or tertiary vessels;
(6) the GFR determined by $^{99m}$Tc-DTPA technology (diethylenetriaminepentaacetic acid) and renal functions were normal.

The exclusion criteria of the study were as follows:

(1) patients with solitary kidneys;
(2) patients with a pathological diagnosis of urothelial carcinoma;
(3) patients with a preoperative history of at least 1 side kidney with a history of injury or other diseases;
(4) patients with special comorbidities effect on renal function, such as hypertention and diabetes mellitus.

Since these procedures were performed at different time periods, only patients who met the inclusion criteria and were treated by the same surgeon that could perform all the procedures skillfully were included in the study.

The data of the preoperative cases were obtained from the inpatient cases, which included gender, age, operation time, time of renal artery blocking, site and size of the tumor, pathological diagnosis, volume of the affected kidney, and GFR of the affected kidney. Patients were followed up through correspondence and visits in the Outpatient Department at the 3rd, 6th, 12th, 24th, and 60th month after the operation. The 320-row volume computed tomography (320CT) and renogram were obligatory examinations to understand the renal function, tumor recurrence, and metastasis.

The preoperative affected GFR ($aGFR_{pre}$), postoperative affected GFR ($aGFR_{post}$), preoperative affected renal volume ($aVol_{pre}$), and postoperative affected renal residual volume ($aVol_{post}$) were collected at during the follow-up period. The correlation between $aGFR_{post}/aGFR_{pre}$ and $aVol_{post}/aVol_{pre}$ were compared.

A series of studies for neonates concluded that the number of nephrons determines renal function,[26] the number of nephrons was fixed after 36 weeks of the fetal period,[26–28] and there was no difference between adults and children.[26,28] Furthermore, the feasibility and reliability of using the ellipsoid method to measure the volume of the kidney in CT was studied.[29] That is, renal length, lateral diameter, and anterior–posterior diameter were measured by abdominal CT using the formula: kidney volume ($cm^3$) = length diameter (cm) × lateral diameter (cm) × anterior–posterior diameter (cm) × $\pi/6$. The preoperative and postoperative renal volumes were measured using this method (Fig. 1).

### 2.2. Statistical analysis

All statistical analyses were performed using SPSS software package, version 22.0. Quantitative data were presented as mean ± standard deviation, and compared using the paired-sample *T* test. The effects of the body mass index (BMI), operation time, WIT and distance from tumor to renal hilum on renal function were analyzed by multivariate linear regression analysis. The correlation between renal function and renal volume was compared using the Pearson product-moment correlation. Overall survival (OS) was defined as the percentage of surviving patients, and disease-free survival (DFS) was defined as the percentage of healthy patients after the 5-year follow-up. OS and DFS were evaluated by Kaplan–Meier survival analysis. $P < .05$ was considered statistically significant.

## 3. Results

After applying a series of criteria, a total of 39 SRPNs were selected for the cohort. The tumor distance from the renal hilum was 3.7 ± 0.4 cm, and the WIT of the selective segmental renal artery was 23.3 ± 3.0 min. The mean tumor size was 3.3 ± 0.5 cm.

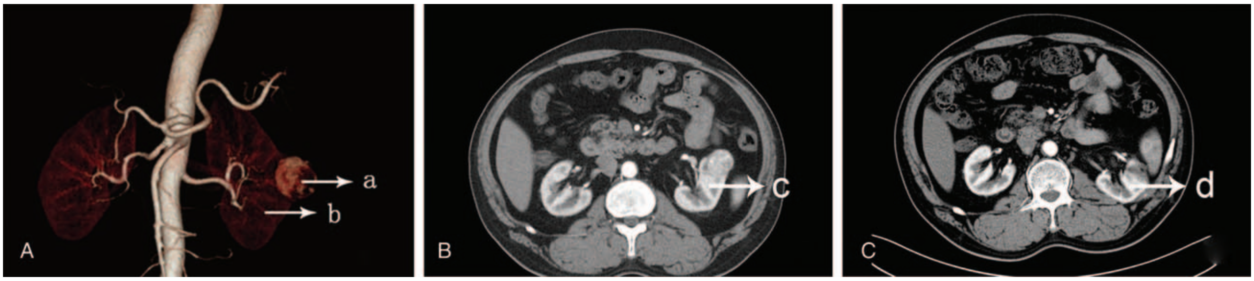


**Figure 1.** Renal tumor and residual renal volume. (A 51-year-old female patient that has been diagnosed with tumor in the left kidney in CTA and enhanced-CT examination shows that the blood supply for the tumor is mainly from the tertiary segmental artery of the left kidney. A CTA; B preoperative enhanced-CT; C postoperative enhanced-CT; (a) renal tumor volume; (b) affected renal volume; (c) $aVol_{pre}$; (d) $aVol_{post}$). $aVol_{post}$ = postoperative affected renal residual volume, $aVol_{pre}$ = preoperative affected renal volume, CT = computed tomography, CTA = computed tomography angiography.

Furthermore, 17 (51.5%) patients were diagnosed with renal clear cell carcinoma, 5 (15.2%) patients were diagnosed with renal papillary carcinoma, 3 (9.1%) patients were diagnosed with chromophobe renal carcinoma, and 8 (24.2%) patients were diagnosed with angiomyolipoma, according to pathology. Moreover, $aVol_{pre}$ was $141.2 \pm 28.8\,cm^3$, and $aGFR_{pre}$ was $45.0 \pm 4.9$ ml/min. The patient characteristics and surgical outcomes of SRPNs for the total cohort are presented in Table 1.

During the follow-up period, 3 patients refused to continue the reviews in the 12th, 22nd, and 24th month after surgery (3 cases were diagnosed as angiomyolipoma, papillary carcinoma, and angiomyolipoma, respectively), a car accident occurred in 1 patient with renal contusion on the 30th month after surgery (diagnosed as chromophobe renal carcinoma), 1 patient relapsed after the 38th month (diagnosed as papillary carcinoma), and 1 patient was detected to have ureteral calculi in the 51st month after surgery (diagnosed as renal clear cell carcinoma). Furthermore, 33 patients were successfully followed up, with an 84.6% follow-up rate. OS was 100% and DFS was 91.7% (95% CI: 57.1–61.3%; Fig. 2).

At 3, 6, 12, 24, and 60 months, $aVol_{post}$ was $101.1 \pm 20.2$, $101.7 \pm 19.6$, $102.2 \pm 20.1$, $102.5 \pm 20.1$, and $102.9 \pm 20.6\,cm^3$, respectively, $aVol_{post}/aVol_{pre}$ was $72.0 \pm 6.6\%$, $72.4 \pm 6.5\%$, $72.8 \pm 6.6\%$, $73.0 \pm 6.6\%$, and $73.2 \pm 6.6\%$, respectively, $aGFR_{post}$ was $34.6 \pm 4.6$, $34.7 \pm 4.8$, $34.9 \pm 4.4$, $35.1 \pm 4.4$, and $35.2 \pm 4.2$ ml/min, respectively (Fig. 3), and the absolute reduction of aGFR was $10.4 \pm 2.3$, $10.4 \pm 2.6$, $10.1 \pm 2.4$, $9.9 \pm 2.4$, and $9.8 \pm 2.5$ ml/min, respectively. Furthermore, $aGFR_{post}$ decreased, compared to that in the preoperative period to a different extent, and the difference was statistically significant ($P < .05$, Table 2). Multivariate linear regression analysis revealed that BMI, operation time, WIT and tumor distance from the kidney had no effect on $aGFR_{post}$ (Table 3, $P > .05$). The correlation coefficients between $aGFR_{post}/aGFR_{pre}$ and $aVol_{post}/aVol_{pre}$ were 0.659, 0.667, 0.663, 0.629, and 0.604, respectively (Table 4), and the difference was statistically significant (Table 3). Moreover, $aGFR_{post}/aGFR_{pre}$ and $aVol_{post}/aVol_{pre}$ had a strong correlation in this cohort, according to the experimental data.

**Table 1**

**The patient's characteristics and the surgical outcomes.**

| | |
|---|---|
| Male/female ratio | 14/19 |
| Patient's age, yr | 52.5 ± 11.8 |
| Body mass index, kg/m$^2$ | 24.1 ± 3.1 |
| Operative time, min | 108.4 ± 9.1 |
| Warm ischemia time, min | 23.3 ± 3.0 |
| Tumor distance from the renal hilum, cm | 3.7 ± 0.4 |
| Blood loss volume, mL | 55.7 ± 13.5 |
| Pathological results | |
| Renal clear cell carcinoma | 17 (51.5%) |
| Renal papillary carcinoma | 5 (15.2%) |
| Chromophobe renal carcinoma | 3 (9.1%) |
| Angiomyolipoma | 8 (24.2%) |
| Tumor size, cm | 3.3 ± 0.5 |
| Tumor volume, cm$^3$ | 17.8 ± 7.7 |
| Preoperative affected renal volume, cm$^3$ | 141.2 ± 28.8 |
| Preoperative affected GFR, mL/min | 45.0 ± 4.9 |

GFR = glomerular filtration rate.

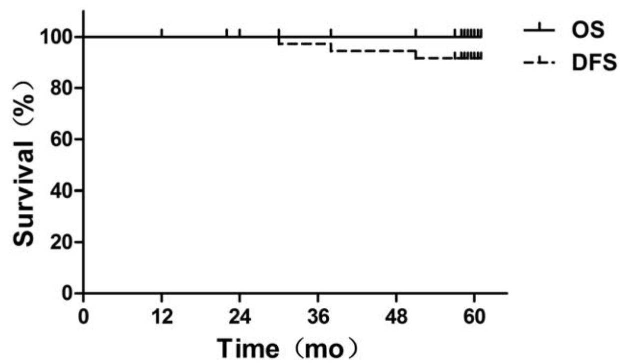


**Figure 2.** Kaplan–Meier curves of the survival of patients.

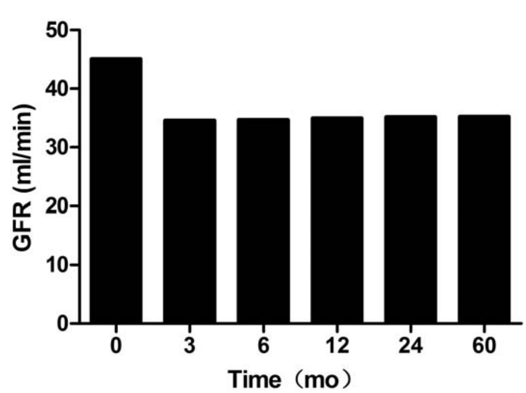


**Figure 3.** The absolute value of postoperative aGFR. aGFR = affected renal glomerular filtration rate.

**Table 2**

**Comparison of preoperative and postoperative aGFR.**

| Variable | 3 mo | 6 mo | 12 mo | 24 mo | 60 mo |
|---|---|---|---|---|---|
| aGFR, mL/min | 34.6 ± 4.6 | 34.6 ± 4.8 | 34.9 ± 4.4 | 35.1 ± 4.4 | 35.2 ± 4.2 |
| Absolute change in aGFR, mL/min | 10.4 ± 2.3 | 10.4 ± 2.6 | 10.1 ± 2.4 | 9.9 ± 2.4 | 9.8 ± 2.5 |
| Residual ratio of aGFR, % | 76.8 ± 4.8 | 76.9 ± 5.6 | 77.6 ± 4.6 | 78.1 ± 4.8 | 78.4 ± 4.9 |
| *P* | .000 | .000 | .000 | .000 | .000 |

aGFR = affected renal glomerular filtration rate.

## 4. Discussion

Controlling WIT for less than 40 min is suitable by traditional view.[30,31] Simmons et al considered that the critical value of WIT was 40 min, and going beyond this time wound cause irreversible damage to the kidney.[32,33] However, Gill et al[34] and Shao et al[5] held the opinion that every minute of IRI would damage renal function. The concept of “zero ischemia” was first proposed by Gill et al,[34] in which the segmental renal artery supplying the tumor was only clamped or dissected. Subsequently, Shao et al[5] applied a new surgical method of SRPN, which was recommended in clinic for the treatment to localized renal tumors. Although clamping the blood supply artery of the tumor to ensure the supply for the rest of normal nephrons was an ideal design, this approach remains controversial, because part of the nephron may be clamped, affecting postoperative renal function. With the development of endoscopic and minimally invasive techniques, as well as further in-depth renal vascular anatomy, SRPN have become a traditional surgical approach for treating localized renal tumors in our team. We strive to dissect the branch arteries of the tumor, at least dissecting to the “secondary” arteries. However, not every patient could be dissected of “tertiary” renal blood vessels[35]. Strictly speaking, the ideal “zero ischemia” is unrealistic, and IRI from part of normal nephrons remains inevitable. Based on the achievements in the past, the present study attempted to explore the correlation between affected renal function and affected renal residual volume, analyzing the causes of decreased renal function. Was the effect of IRI induced by intraoperative segmental renal arterial clamping, or the decreased inherent nephrons from the removal of part of these nephrons?

“Pseudocapsule enucleation” of the renal tumor has been highlighted in recent years. The main point of “pseudocapsule enucleation” was that a natural dissection plane was formed on the tumor tissue and its surrounding healthy renal parenchyma, and along this plane, a blunt dissection would complete the removal of the tumor.[36–38] This approach can reduce the positive margin and preserve more renal parenchyma.[39,40] The potential invasion to the pseudocapsule of the localized renal tumor makes this method have relative indications.[41,42] In low-grade tumors, “pseudocapsule enucleation“ oncology outcomes were equivalent to PN,[40] and it turned out that this surgical approach does not affect the positive margin rate, local recurrence, and survival.[43,44] Takagi et al[45] applied a 0.5-cm margin for less than 4 cm of the renal tumor, and confirmed that the positive margin rate had no significant difference between the “pseudocapsule enucleation” and PN. Oh et al[46] concluded that the margin is the most important factor of local recurrence, and an adequate visible margin guaranteed the complete removal of the tumor. Li et al[47] considered that a surgical margin of 0.5 cm was enough to prevent the local recurrence of the tumor. For localized renal carcinoma that underwent PN, the larger margin increased the difficulty of operation, induced the over-resection of nephrons, and increased morbidity due to complications, resulting in the decline of renal function.[44,46–48] The indications and margin of the “pseudocapsule enucleation” remains controversial. A technology was used for electrocoagulating tissues, providing a line of approximately 0.5 cm from the edge of the tumor, allowing the tumor to be removed intact. According to the pathological diagnosis, all surgical margins were negative. The 5-year OS was 100% and the 5-year DFS was 91.7% (95% CI: 57.1–61.3%). Merely 1 patient

**Table 3**

**The multivariate linear regression analysis for $aGFR_{post}$.**

| | 3 mo | | 6 mo | | 12 mo | | 24 mo | | 60 mo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Variation | B | *P* | B | *P* | B | *P* | B | *P* | B | *P* |
| BMI | −0.212 | .476 | −0.233 | .457 | −0.142 | .622 | −0.173 | .546 | −0.224 | .419 |
| Operation time | −0.045 | .655 | −0.047 | .652 | −0.060 | .539 | −0.066 | .499 | −0.031 | .740 |
| WIT | −0.230 | .452 | −0.271 | .400 | −0.181 | .541 | −0.117 | .692 | −0.194 | .496 |
| Tumor distance from the renal hilum | 0.101 | .959 | 0.682 | .744 | 0.259 | .893 | −0.178 | .926 | −0.293 | .874 |

$aGFR_{post}$ = postoperative affected GFR, BMI = body mass index, WIT = warm ischemic time.

**Table 4**

**The correlation between $aGFR_{post}/aGFR_{pre}$ and $aVol_{post}/aVol_{pre}$.**

| Time | 3 mo | 6 mo | 12 mo | 24 mo | 60 mo |
|---|---|---|---|---|---|
| $aGFR_{post}/aGFR_{pre}$ (%) | 76.8 ± 4.8 | 76.9 ± 5.6 | 77.6 ± 4.6 | 78.1 ± 4.8 | 78.4 ± 4.9 |
| $aVol_{post}/aVol_{pre}$ (%) | 72.0 ± 6.6 | 72.4 ± 6.5 | 72.8 ± 6.6 | 73.0 ± 6.6 | 73.2 ± 6.6 |
| *R* | 0.659 | 0.667 | 0.663 | 0.629 | 0.604 |
| *P* value | .000 | .002 | .000 | .000 | .000 |

$aGFR_{post}$ = postoperative affected GFR, $aGFR_{pre}$ = preoperative affected GFR, $aVol_{post}$ = postoperative affected renal residual volume, $aVol_{pre}$ = preoperative affected renal volume.

relapsed after the 38th month, in which the histopathologic diagnosis was papillary carcinoma. The early detection and treatment of localized renal tumor can improve the excellent prognosis of patients. Furthermore, the necessary postoperative follow-up can prolong the survival of patients and improve their quality of life.

Compared to preoperative effects on renal function, postoperative affected renal function decreased during the whole follow-up period ($P < .05$). BMI, operation time, WIT, and tumor distance from the kidney had no effect on $aGFR_{post}$ ($P > .05$). The reason was that the tumor was part of the nephrons, and the removal of the tumor caused the lack of inherent nephrons, resulting in loss of renal function. The $aGFR_{post}$ remains essentially unchanged ($P > .05$), indicating that the loss of inherent nephrons led to decreased renal function. However, this had no impact on IRI.

The correlation coefficients between $aGFR_{post}/aGFR_{pre}$ and $aVol_{post}/aVol_{pre}$ ranged from 0.604 to 0.667 ($r > 0.5$), and the statistical data were positively correlated. Furthermore, the difference was statistically significant ($P < .05$), and postoperative affected renal function and affected renal volume both had a good correlation. This implies that postoperative affected renal function is associated with affected renal volume after the operation. The IRI induced by intraoperative segmental renal arterial clamping less likely affected postoperative renal function.

In summary, the prognosis was excellent with prolonged survival after the 5-year follow-up period for patients who received SRPN for localized renal tumors. However, this affected renal function deterioration after the operation, because the tumor was a part of the nephrons. IRI induced by the temporary SRPN during the operation could not compromise for long-term postoperative renal function, which is mainly associated with the affected renal volume. We should shorten the margin and maintain nephrons as much as possible during the operation before completely removing the tumor, in case excessive excision of inherent nephrons occurs, preventing the unnecessary loss of renal function.

Several limitations of the study should not be ignored. We have no data on patients before suffering from the renal tumor. Furthermore, the present study had a small cohort size, and the outcomes would be more ideal if studies with a large sample size could be conducted, and further research with a long-term follow-ups could be carried out. Additionally, there was a lack of evaluation in the molecular level about detecting damaged renal function, such as Neutrophil Gelatinase-Associated Lipocalin and Kidney Injury Molecule-1 in serum and urinary[49] in the study.

In SRPN, the resection of the tumor as a part of nephrons cause parenchymal loss, resulting in renal function deterioration, rather than the outcomes of IRI. Postoperative affected renal function should be considered with the affected renal parenchymal volume. We should do our best to maintain more nephrons before we could completely resect the tumor, in case of unnecessary loss of renal function.

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**Writing – original draft:** Fang-Min Chen, Rui-Jie Hu, Xi-Nan Jiang.
**Writing – review and editing:** Fang-Min Chen, Rui-Jie Hu, Si-Wen Zhong, Shuai Tang.

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